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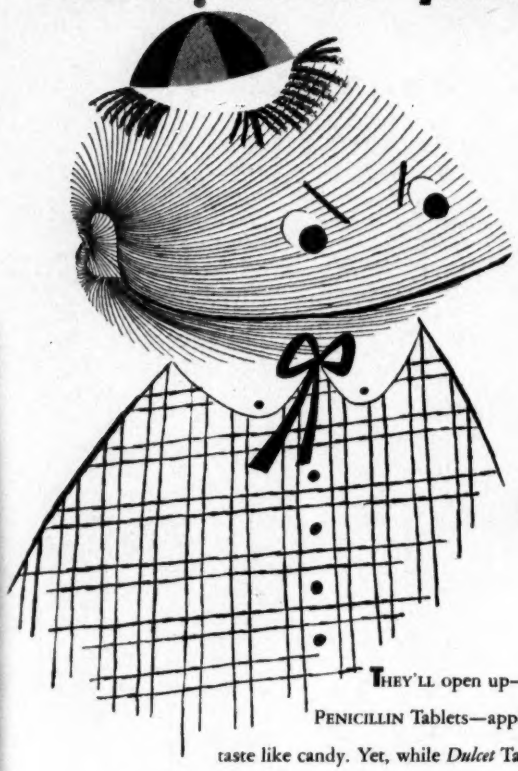

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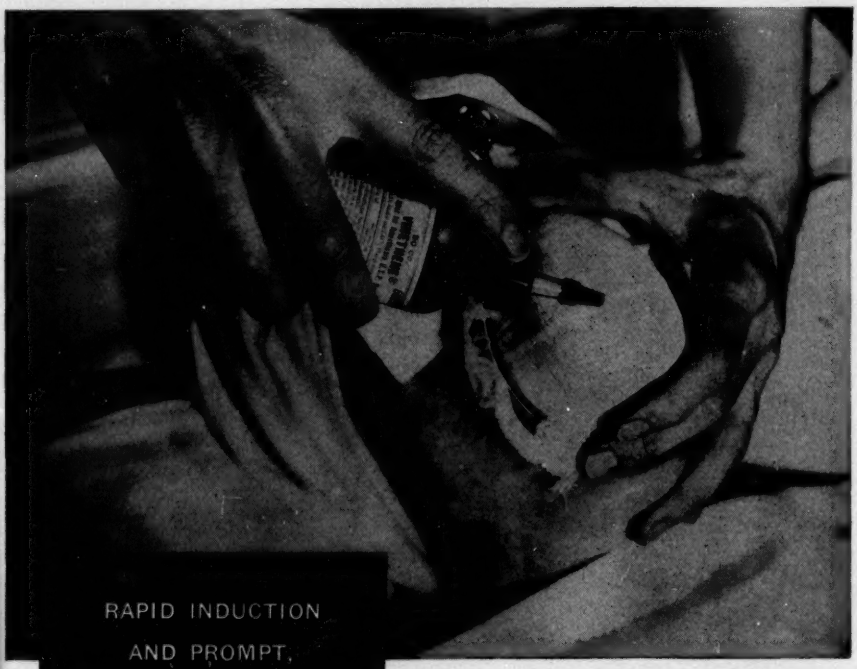

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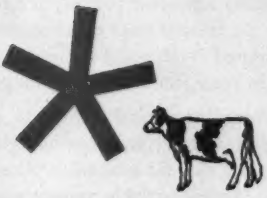

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1. Clein, N.W.: Cow's Milk Allergy in Infants, *Annals of Allergy*, 9:195, 1951.

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1. Cannon, P. R.: The Importance of Proteins in Resistance to Infection, J. A. M. A. *128*:360 (June 2) 1945.

2. Strumia, M. M., and Boerner, F.: Phagocytic Activity of Circulating Cells in the Various Types of Leukemia, Am. J. Path. *13*:335 (May) 1937.

3. Mills, C. A., and Cottingham, E.: Phagocytic Activity as Affected by Protein Intake in Heat and Cold, J. Immunol. *47*:503 (Dec.) 1943.

4. Elman, R., and Cannon, P. R.: Protein Malnutrition, in Jolliffe, N.; Tisdall, F. F., and Cannon P. R.: Clinical Nutrition, New York, Paul B. Hoeber, Inc., 1950, chap. 7, p. 192.

5. McLester, J. S.: Nutrition and Diet in Health and Disease, ed. 5, Philadelphia, W. B. Saunders Company, 1949, p. 347.

6. Cannon, P. R.: Recent Advances in Nutrition with Particular Reference to Protein Metabolism, Lawrence, Kansas, Univ. of Kansas Press, 1950, p. 19.

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1. Am. J. Pub. Health 37:1113
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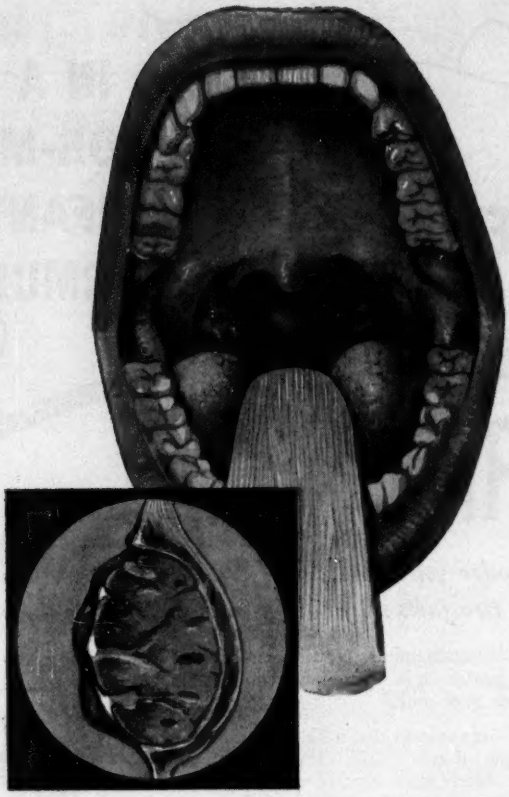

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Sayer, R. J.; Michel, J.; Moll, F. C., and Kirby, W. M. M.: Am. J. M. Sc. 221:256 (March) 1951

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References

1. Clinical Nutrition: ed. by N. Jolliffe et al., Hoeber, 1950. 2. Hanke M. T.: Diet and Dental Health, Chicago Univ. Press, 1933. 3. Jeans, P. C.: J.A.M.A., 142:806, 1950. 4. Joslin C. L. and Bradley, J. E.: Personal communication. 5. Krehl, W. A. and Cowgill, G. R.: Food Research, 15:179, 1950. 6. McLester, J. S.: Nutrition and Diet in Health and Disease, Saunders, Phila., 4th ed., 1944. 7. Moore, E. L. et al.: J. Home Econ., 37:290, 1945. 8. Roy, W. R. and Russell, H. E.: Food Industries, 20:1764, 1948. 9. Sherman, H. C.: Chemistry of Food and Nutrition, Macmillan, 7th ed., 1946. 10. Silverman, A. C.: New York J. Med., 47:1987, 1947. 11. Stevenson, S. S.: J. Pediat., 31:616, 1947.

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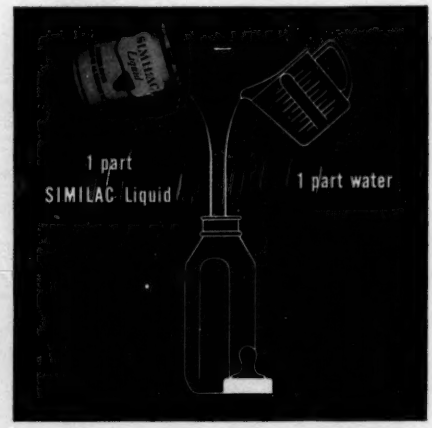

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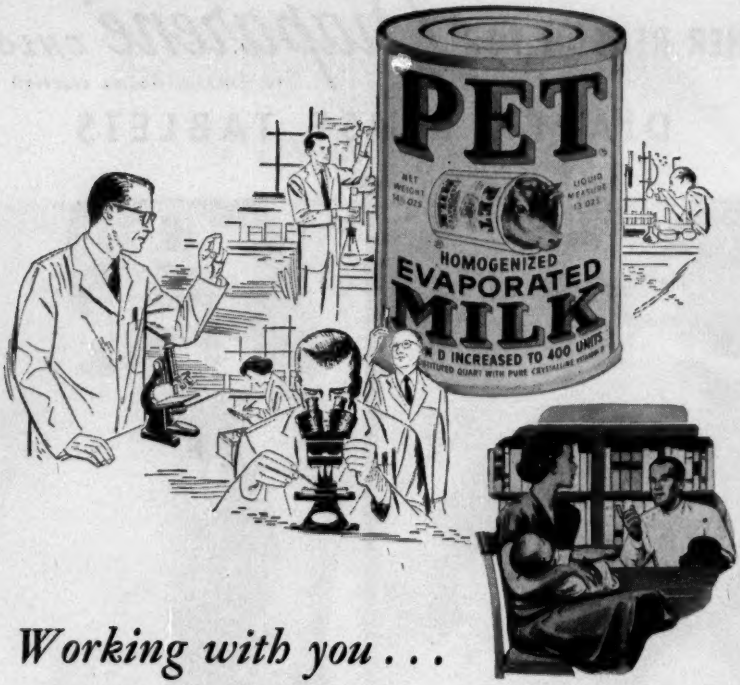

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American Journal of Diseases of Children

VOLUME 82 DECEMBER 1951 NUMBER 6

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SPECIFIC TREATMENT OF CHILDREN WITH TUBERCULOSIS

EDITH M. LINCOLN, M.D.
AND
VIRGINIA N. WILKING, M.D.
NEW YORK

ONE HUNDRED and seventy-two children have been treated with various tuberculostatic agents during the last four and one-half years in the tuberculosis ward of the children's medical service of Bellevue Hospital. It is the purpose of this paper to state the indications for the use of chemotherapy which are used in this service, to outline the methods of treatment used for different forms of tuberculosis, and to give some results of treatment. No attempt will be made to compare results with those obtained by other investigators or with different forms of treatment.

The basis of selection of cases for therapy must be an understanding of the course and prognosis of the disease to be treated. New forms of therapy, especially if potentially toxic, are usually first used in forms of disease which have a high fatality rate. An analysis of the deaths [1] in a series of 622 consecutive cases of primary pulmonary tuberculosis seen in the children's chest clinic of Bellevue Hospital between 1930 and 1940 demonstrated that four complications, occurring in about 20% of the ward population, accounted for 95% of the fatalities. Meningitis was always fatal in this series; every patient with acute generalized miliary tuberculosis ultimately died of tuberculosis; about two-thirds of the cases of protracted forms of hematogenous tuberculosis ended fatally, and the case fatality rate was about the same in children showing evidence of locally progressive primary tuberculosis with cavitation and bronchogenic spread. Deaths from these causes usually took place within a year from the first diagnosis of tuberculous disease and were called deaths from primary tuberculosis. Because of this previous experience, children with any of these four complications were placed on chemotherapy as soon as the diagnosis was made.

Another frequently fatal form of tuberculosis was reinfection pulmonary tuberculosis, occurring most commonly in the group 8 to 12 years old and ending fatally within five years in more than 50% of the cases. The case fatality rate was much lower among patients seen initially with a minimal lesion than among children first

From the Chest Clinic of the Children's Medical Service, Bellevue Hospital, and the Department of Pediatrics, New York University College of Medicine.

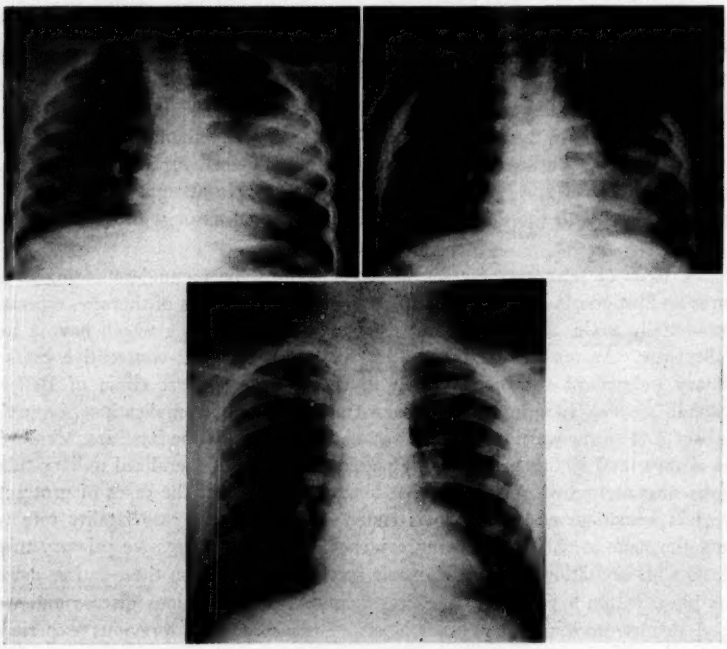
Aided by the National Tuberculosis Association, the Division of Research Grants and Fellowships of the National Institutes of Health, United States Public Health Service, and Parke, Davis & Company, Detroit.

1. Lincoln, E. M.: Course and Prognosis of Tuberculosis in Children, Am. J. Med. 9:623 (Nov.) 1950.

seen with moderately or far-advanced tuberculosis. The use of streptomycin for chronic pulmonary tuberculosis was therefore limited to patients with more than minimal disease.

To patients with the five forms of tuberculosis discussed above streptomycin was given as a lifesaving measure. This group constituted approximately 20% of the ward population from December, 1946, to May 1, 1951, the period of this report.

The remaining patients fell into two groups: one in which chemotherapy was used as an elective measure and one in which the use of chemotherapy seemed contraindicated.



Roentgenograms of a 2-year-old child with primary pulmonary tuberculosis treated with streptomycin: Above left, appearance of lung fields at onset of disease, November, 1947; 1 gm. of streptomycin was given daily for 90 days. Above right, in May, 1948, six months after onset of primary tuberculosis, minimal change in size of primary complex. Below, in April, 1951, calcification in left root with faint shadows still present in mid-left-lung field.

The first of these two groups, the one for which the use of specific treatment was elective, was composed of approximately 10% of the patients in the ward. Here streptomycin was given not in an attempt to avoid a fatal outcome but rather in an attempt to improve the end-result and shorten the period of hospitalization. In this group we have treated tuberculous otitis and cervical adenitis, endobronchial disease secondary to primary tuberculosis, tuberculous laryngitis, and bone and joint tuberculosis; we have also used streptomycin to "cover" surgical procedures. We treated these patients either to learn whether the complications under consideration

would respond to treatment or because the use of chemotherapy had been reported favorably by other observers. It is obvious that criteria for treatment in this group will change as results of therapy are reevaluated, especially after late follow-up. For instance, in the group of children with primary tuberculosis complicated by the presence of endobronchial tuberculosis, a review of 30 cases showed no evidence of definite response to therapy, and therefore in the future children with endobronchial disease will not be treated routinely. Indications for treatment will also change as new effective drugs become available.

In addition to the first group of cases, in which specific therapy is always indicated, and the second group, in which chemotherapy is an elective procedure, there remains a third group of children, representing about 70% of our ward population, for which we believe the use of streptomycin is contraindicated at the present time. This group includes patients with uncomplicated primary tuberculosis and minimal chronic pulmonary tuberculosis. In our service the size of a pulmonary primary complex or the youth of the patient is not used as an indication for specific therapy of uncomplicated primary tuberculosis. We arrived at this decision because we could obtain no evidence that the resolution of the primary pulmonary focus had been hastened by the use of streptomycin in children treated intensively by us for miliary tuberculosis or tuberculous meningitis. Similar results have been reported elsewhere.[2] Additional evidence against the advisability of treatment of primary tuberculosis was secured from review of the early roentgenograms of children treated specifically for primary tuberculosis elsewhere, who were later seen by us (Figure). A second reason for not treating uncomplicated primary tuberculosis is the absence of evidence that streptomycin prevents the development of complications. In common with many other observers, we have seen meningitis develop after intensive specific therapy for miliary tuberculosis and have watched tuberculous complications in bones, nodes, and other areas develop and progress while the patient was under streptomycin therapy for other forms of tuberculosis. There is definite evidence that specific treatment of primary tuberculosis does not preclude the later development of meningitis.[3] A third reason for witholding streptomycin is the possibility of the emergence of organisms resistant to streptomycin, which might limit its later effective use. This is particularly important in primary tuberculosis, because it is in the early phases of tuberculosis that meningitis and miliary tuberculosis are most likely to occur.

METHODS OF TREATMENT

In the group of patients with meningitis, miliary tuberculosis, or both, our present scheme of treatment is essentially the same as that in previous cases reported from this service,[4] and any deviations from the general plan presented have been minor ones (Table 1).

2. Lorber, J.: Streptomycin and the Primary Lung Lesion in Tuberculosis in Children, Lancet **1**:389 (March 4) 1950.

3. Berenberg, W.; Cook, C. D., and Twinam, C. W.: Streptomycin in Pulmonary Tuberculosis in Children, J. A. M. A. **145**:1044 (April 7) 1951.

4. Lincoln, E. M., and Kirmse, T. W.: Streptomycin-Promizole Therapy of Miliary and Meningeal Tuberculosis in Children, Am. Rev. Tuberc. **61**:159 (Feb.) 1950.

Acute Meningitis.—All patients, irrespective of age or weight, are given 1.0 gm. of streptomycin daily intramuscularly; this dose is divided into two daily doses of 0.5 gm. each for infants and for older children who are emaciated. In addition to intramuscular streptomycin, all patients are given thiazolsulfone (promizole®) in divided doses every six hours. Infants receive initially 0.5 gm. daily, while older children are given 1.0 gm. daily. Blood levels are determined before the dose is increased, and if they are unsatisfactory, the daily dose is increased or decreased until a blood thiazolsulfone level of between 1 and 3 mg. per 100 cc. is obtained two and one-half to three hours after the usual dose. Thiazolsulfone is being given for a total of three years to the first 25 patients treated for tuberculous meningitis and for a total of two years to the later patients. Administration of streptomycin intramuscularly is continued daily for a minimum period of six months. In addition, all patients are given a daily intrathecal injection of 100 mg. of streptomycin. At least 40 intrathecal injections are given, and every effort is made to continue the 100 mg. daily for as long as possible. Fifty milligrams is sometimes used for the first intrathecal dose for an infant. Three types of reaction influence the decision

TABLE 1.—*Treatment of Meningitis and Miliary Tuberculosis*

		Dosage	
	Route	Miliary Tuberculosis	Meningitis
Streptomycin	Intramuscular	1.0 gm. daily for 4 mo.	1.0 gm. daily for 6 mo.
Streptomycin	Intrathecal	.....	100-50 mg. for minimum of 40 injections
Thiazolsulfone	Oral	Increased from 0.5 gm. daily until blood level of 1-3 mg. per 100 cc. obtained; range 0.25 to 8 gm. daily every 6 hr.; continued 2-3 yr.	

to decrease the daily intrathecal dose of streptomycin or to increase the interval between intrathecal injections. One is the presence of repeated convulsions closely related in time to intrathecal therapy. A second is an abrupt rise in temperature to 105 F. or more following intrathecal therapy. The third consists of loss of reflexes with extreme lethargy often associated with an alarming accentuation of irregularities of respiratory or cardiac rate. This reaction is important because if prolonged it interferes with nutrition and if severe should always be an indication for modifying treatment. The plan of therapy has not been altered because of the development of increased toxicity, spasticity, hyperreflexia, strabismus, nystagmus, tremors, or vomiting or because a child appeared sicker after the intrathecal injection.

Intrathecal therapy is discontinued after 40 injections only if the cerebrospinal fluid sugar level has been above 40 mg. per 100 cc. for one week, if the base line levels of cells and protein are not rising, and if the clinical condition of the patient is satisfactory. Frequent lumbar taps follow immediately after the completion of intrathecal therapy. Thereafter, weekly lumbar taps are done throughout the course of intramuscular streptomycin therapy and are continued for at least two months after the completion of intramuscular streptomycin therapy.

Relapse of meningitis after the completion of intramuscular therapy has been treated in three patients by repeating the full course of intrathecal and intramuscular streptomycin. Another three patients had a recrudescence of their meningitis after

the course of streptomycin intrathecally had been completed but while they were still receiving streptomycin intramuscularly; a further course of streptomycin intrathecally has been given. In these three cases the course of intrathecally injected streptomycin was prolonged beyond 40 injections and the period of intramuscular injections extended beyond six months. One patient was treated with streptococcic enzymes intrathecally, and another is under treatment with purified protein derivative and streptomycin given intrathecally.

Internal noncommunicating block was treated in four patients. One patient was given streptococcic enzymes by the lumbar route and through ventricular burr holes with transient relief of block followed by death. At autopsy highly organized exudate was found practically obliterating the subdural space. A second patient was given the last four of his 40 injections of streptomycin by the ventricular and cisternal routes after ventriculotomy and has made a good recovery. In two cases tuberculin was used intrathecally according to the method of Smith and Vollum [5] by lumbar or ventricular route after burr holes had been made; one patient died without relief of block, and the other is still under treatment. In all of these cases daily

TABLE 2.—*Results of Treatment of Meningitis and Miliary Tuberculosis*

Diagnosis	No. of Patients	Died	Under Treatment	Survival Time*			
				>6 Mo.	>1 Yr.	>2 Yr.	>3 Yr.
Miliary tuberculosis	16	2†	2	2	5	2	3
Meningitis	28	9	6	1	1	5	6
Combined meningitis and miliary tuberculosis	11	2	2	..	3	1	3
Total patients	55	13	10	3	9	8	12

* Survival time computed from beginning of treatment.
† Including 1 patient admitted for miliary tuberculosis who died of relapse of meningitis previously treated in another hospital.

administration of streptomycin was continued by ventricular, cisternal, or lumbar route as well as by the intramuscular route.

Acute Miliary Tuberculosis.—Streptomycin in a dose of 1.0 gm. is given daily intramuscularly to all age groups for a total of four months. Thiazolsulfone is used as in the treatment of tuberculous meningitis. The first 25 patients are receiving thiazolsulfone for a total of three years, while the later patients are receiving it for two years. One patient found resistant to streptomycin at the start of therapy has been treated with thiazolsulfone and viomycin. Roentgenograms showed that the nodules cleared slowly as with thiazolsulfone therapy,[6] but there was prompt conversion of gastric cultures to negative after viomycin was given.

Acute Miliary Tuberculosis with Meningitis.—Patients who have been admitted with acute miliary tuberculosis and meningitis are treated according to the plan outlined for meningitis alone. Patients in whom meningitis developed in the course of miliary tuberculosis are treated as outlined under meningitis for six months from the date of the diagnosis of meningitis. Results of treatment of meningitis and miliary tuberculosis are shown in Table 2.

5. Smith, H. V., and Vollum, R. L.: Effects of Intrathecal Tuberculin and Streptomycin in Tuberculous Meningitis, Lancet **2**:275 (Aug. 19) 1950.

6. Lincoln, E. M.; Stone, S., and Hoffman, O. R.: The Treatment of Miliary Tuberculosis with Promizole, Bull. Johns Hopkins Hosp. **82**:56 (Jan.) 1948.

Less Fatal Forms of Longer Duration.—Three other forms of tuberculosis, protracted hematogenous tuberculosis, progressive primary tuberculosis, and chronic pulmonary tuberculosis, also had high fatality rates before chemotherapy but were often of longer duration than meningitis and miliary tuberculosis and less surely fatal. There has been some variation in length of treatment and in the selection

TABLE 3.—*Treatment of Protracted Hematogenous Tuberculosis, Progressive Primary Tuberculosis, and Chronic Pulmonary Tuberculosis*

		Dosage		
	Route	Protracted Hematogenous Tuberculosis	Progressive Primary Tuberculosis	Chronic Pulmonary Tuberculosis
Streptomycin	Intramuscular	On weight basis for 2-4 mo.	On weight basis daily for 2-4 mo. or 0.5 to 1 gm. twice weekly indefinitely	On weight basis daily for 2-4 mo. or 0.5 to 1 gm. twice weekly indefinitely
Thiazolsulfone	Oral	Increase from 0.5 gm. daily until blood level of 1-3 mg. per 100 cc. obtained; continued for 1 yr.	.....	.....
Paraaminosalicylic acid	Oral	.....	0.5 gm./kg. daily	0.5 gm./kg. daily

TABLE 4.—*Dose of Streptomycin on Weight Basis*

Wt. of Patient	Daily Dose, Gm.
Less than 10 lb.	0.3
10-19 lb.	0.4
20-39 lb.	0.5
40-59 lb.	0.6
60-89 lb.	0.75
90 lb. or over	1.0

TABLE 5.—*Results of Treatment of Patients with Protracted Hematogenous Tuberculosis, Progressive Primary Tuberculosis, and Chronic Pulmonary Tuberculosis*

Diagnosis	No. of Patients	Died	Under Treatment	Survival Time			
				>6 mo.	>1 Yr.	>2 Yr.	>3 Yr.
Protracted hematogenous tuberculosis	8	..	1	1	3	..	3
Progressive primary tuberculosis	22	..	2	6	4	6	4
Chronic pulmonary tuberculosis	24	1*	5	2	3	6	7

* Died at home 2 mo. after removal from hospital against advice.

of drugs in these forms of tuberculosis. The treatment schedules given in Tables 3 and 4 are the ones used most commonly and represent the scheme of treatment we use at present. The number of patients treated and their follow-up data are shown in Table 5.

Protracted Hematogenous Tuberculosis.—Streptomycin was usually given in combination with thiazolsulfone, in one case with paraaminosalicylic acid; one child was given paraaminosalicylic acid alone. After administration of streptomycin was discontinued, thiazolsulfone or paraaminosalicylic acid was continued as the sole chemotherapeutic agent for a total period of not more than one year.

Progressive Primary Tuberculosis.—These patients all had roentgenographic evidence of a primary focus with cavitation and bronchogenic spread. The series includes two patients treated only with streptomycin and one treated only with paraaminosalicylic acid. Originally the streptomycin was given for periods of two to four months. The dose of thiazolsulfone was as usual regulated by the blood level; paraaminosalicylic acid was given on a weight basis: 0.5 gm. per kilogram daily by mouth every four hours, up to a daily dose of 12.0 gm. Blood levels on this dosage of paraaminosalicylic acid ranged from 4 to 9 mg. per 100 cc. taken one and one-half to two and one-half hours after a single dose was given. The secondary drug was continued after streptomycin had been stopped, usually for a total of one year. We now tend to use paraaminosalicylic acid as the secondary drug in all cases of progressive primary tuberculosis, reserving thiazolsulfone for children with marked evidence of spread of their disease by the hematogenous route. Many of these patients have residual cavities and will probably require surgical resection to control their disease. Therefore, recent patients are now being given combined therapy, the intention being to continue it for an indefinite period, a procedure reported by D'Esopo for cases of chronic pulmonary tuberculosis.[7] Patients on long-term therapy are now receiving streptomycin twice weekly and paraaminosalicylic acid daily, as it has been shown that a similar scheme of treatment is as effective as daily streptomycin in chronic pulmonary tuberculosis [8] and delays the emergence of resistance.[9]

Chronic Pulmonary Tuberculosis.—The plan of treatment in this group has been similar to the treatment of children with progressive primary tuberculosis. Four patients were treated with streptomycin alone and two with paraaminosalicylic acid alone. Five patients were treated with streptomycin and thiazolsulfone, and seven of the earlier and all of the later patients have been treated with streptomycin and paraaminosalicylic acid. In two cases sufficient clearing followed initial treatment with streptomycin that successful collapse therapy with pneumothorax could be established. In one case pneumoperitoneum was performed. In one case a modified thoracoplasty followed streptomycin therapy, and to date two children have had surgical resections of their pulmonary disease.

Other Forms.—Sixty-three other patients were treated with various agents. All received streptomycin except for four patients who were treated for tuberculous cervical adenitis by incision and drainage and local instillation of streptococcic enzymes and two patients with endobronchial disease who received only paraaminosalicylic acid. This group included 30 patients with tuberculous endobronchial disease associated with primary tuberculosis, 10 with tuberculous adenitis, 9 tuberculous children "covered" with streptomycin during surgical procedures, and 5 patients treated for tuberculosis of the bones or joints. Streptomycin was usually

7. D'Esopo, N. D.: Prolonged Chemotherapy of Pulmonary Tuberculosis: Preliminary Report, Minutes of the Eighth Streptomycin Conference Held on Nov. 10, 11, 12, and 13, 1949, Fulton County Medical Society, Atlanta, Georgia, prepared and edited by Veterans Administration Area Office, Washington, D. C.

8. Tempel, C. W.; Hughes, F. J., Jr.; Mardis, R. E.; Towbin, M. N., and Dye, W. E.: Combined Intermittent Regimens Employing Streptomycin and Para-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis, Am. Rev. Tuberc. **63**:295 (March) 1951.

9. Dye, W. E.: Streptomycin-Resistant Tubercle Bacilli: Incidence in Cases Treated with Different Dosage Schedules, Am. Rev. Tuberc. **67**:719 (May) 1950.

given as the sole chemotherapeutic agent only when the total period of treatment did not exceed three weeks, as in the treatment of laryngitis or when it was used as a precautionary measure in surgery. Otherwise, streptomycin was given only in combination with paraaminosalicylic acid or thiazolsulfone. Streptomycin was given according to the patients' weight (Table 4), thiazolsulfone and paraaminosalicylic acid as for other forms of tuberculosis. The duration of combined therapy varied from six weeks to three months.

COMMENT

The death rate should in part reflect the efficacy of treatment in the group of children for whom we consider the use of streptomycin to be mandatory. In the two years prior to the use of streptomycin the death rate in the children's tuberculosis ward from complications of primary tuberculosis was 18%. Since the introduction of streptomycin the death rate from primary tuberculosis has been

TABLE 6.—*Stage of Meningitis in Relation to Mortality*

Stage	No. of Patients	Deaths
Early	21	3
Moderately advanced	8	2
Late	10	6

TABLE 7.—*Age in Relation to Mortality from Tuberculous Meningitis*

Age	No. of Patients	Deaths
Under 1 yr.	10	5
1-2 yr.	15	4
3-5 yr.	10	2
6-12 yr.	4	..

under 3%. With the exception of one death due directly to miliary tuberculosis, all the deaths from primary tuberculosis have been due to meningitis. One child died of chronic pulmonary tuberculosis two months after she left the hospital against advice. But more than mere survival is desired. Successful therapy should mean an eventual resumption of normal life for the child. The meningitis patients who survived three months after streptomycin therapy was discontinued have all remained well, and there have been no late relapses. Seven of the meningitis patients are deaf; three have residual hemiplegias, and one has a foot drop. Otherwise there have been no neurological sequelae. A final evaluation of the survivors from a psychiatric and psychologic viewpoint is impossible without a longer follow-up period, but we hope to make an interim report on these aspects in the near future.

The results of therapy in meningitis would seem to depend partly on the stage of meningitis when it is first diagnosed and to a less extent on the age of the child when meningitis is discovered (Tables 6 and 7). Tuberculous meningitis before therapy was used was a disease of short duration, the average patient surviving only 19½ days in our experience.[10] It is inevitable that patients for whom

10. Lincoln, E. M.: Tuberculous Meningitis in Children: With Special Reference to Serous Meningitis; Tuberculous Meningitis, Am. Rev. Tuberc. **56**:75 (Aug.) 1947.

a late diagnosis is made will have a poorer chance of survival and that some of those who survive will have suffered irreversible brain damage. Prompt diagnosis must therefore be a forerunner of successful therapy, and, as a corollary to this, treatment should be prompt and energetic. Intensive therapy, including daily intrathecal administration of streptomycin in the maximum amounts tolerated, is important in the early days of treatment. The ultimate fate of the patient may well be decided by the intensity of early treatment. The value of intrathecal therapy has been adequately demonstrated.[11] The survival rate of published series of cases in which intramuscular therapy alone was given does not compare favorably with series in which treatment consisted of combined intrathecal and intramuscular injections of streptomycin. Prolonged therapy is also important, especially when meningitis is associated with pulmonary tuberculosis or an active extrapulmonary focus of tuberculosis.[12] The total period of streptomycin therapy may perhaps be shortened by the concurrent use of a secondary drug which is bacteriostatic, but certainly six months should be considered a minimum period of treatment with intramuscularly given streptomycin. Moreover, the prolonged use of the secondary drug beyond the period of streptomycin therapy may help in preventing late relapse of meningitis. Recrudescence of meningitis while the patient is still receiving streptomycin intramuscularly or relapse within weeks after use of streptomycin has been discontinued can be diagnosed early only by frequent lumbar punctures during the period of observation and therefore necessitates close supervision of the patient, preferably in the hospital. Frequent examination of the cerebrospinal fluid in the course of miliary tuberculosis is also necessary if meningitis is to be diagnosed promptly. There is still a need for new methods of treatment in order to ensure the survival of a larger percentage of children. The intrathecal use of tuberculin offers a new approach to this problem, and results reported from Oxford give hope that the number of patients surviving tuberculous meningitis with recovery of all faculties will be increased.

Longer periods of follow-up will be necessary before there can be final evaluation of the results of therapy of progressive primary tuberculosis and chronic pulmonary tuberculosis. With one exception (Table 5) our patients have survived, and many have made remarkable clinical recoveries. In some the change from a picture of emaciation and chronic illness to that of a healthy child has been striking. Residual cavitation or other evidence of residual disease has, however, persisted on roentgenograms in some cases, and it seems probable that surgery may be needed finally to eradicate the menace of chronic disease. Long-term plans must be made if these children are to be saved from a deferred death or from long invalidism. From the evidence presented by D'Esopo and Medlar, it is evident that chemotherapy can often be prolonged with benefit, especially when ultimate surgery is under consideration.

Combined therapy is indicated whenever streptomycin therapy is continued for more than three weeks, because it has been shown to delay the emergence of tubercle bacilli resistant to streptomycin; moreover, the value of each drug is enhanced by the combination. Thiazolsulfone has been used with streptomycin when the control

11. British Medical Research Council: Streptomycin Treatment of Tuberculous Meningitis: Streptomycin in Tuberculosis Trials Committee, Lancet **1**:582 (April 17) 1948.

12. Cairns, H.; Smith, H. V., and Vollum, R. L.: Tuberculous Meningitis, J. A. M. A. **144**:92 (Sept. 9) 1950.

of disease of lymphohematogenous origin was the main problem, paraaminosalicylic acid with progressive primary or reinfection tuberculosis. With the exception of one patient with exfoliative dermatitis seen in 1948, no severe toxic reaction to streptomycin intramuscularly has been observed. Loss of vestibular function occurs in practically every case but is apparently reversible. Deafness has occurred only in patients with tuberculous meningitis treated intrathecally with streptomycin and has not been reversible. Toxic reactions to streptomycin intrathecally have never been so severe as to require discontinuance of treatment. Toxic reactions to thiazolsulfone have not been troublesome and have been discussed in previous papers.[13] Paraaminosalicylic acid is remarkably well tolerated by children when given in proper dosage.

In the group of cases in which specific treatment is an elective measure, the type of case in which there should be treatment and the method of treatment will undoubtedly change as new effective drugs become available. Chemotherapy should not be used unless a drug is likely to cure symptoms and eliminate evidence of disease more quickly and effectively than would happen without specific treatment. Proof of rapid response to streptomycin is often obtained incidentally when a tuberculous lesion heals although therapy was not primarily directed to it. The rapid healing of cutaneous sinuses overlying tuberculous bone disease and of tuberculous laryngitis and endobronchial disease associated with chronic pulmonary tuberculosis makes it desirable to treat these forms of tuberculosis with short courses of streptomycin even if the basic tuberculous disease is not affected by the treatment. On the other hand, the routine use of streptomycin in tuberculous cervical adenitis is not advised, since in our experience the response to therapy has been variable and the results not sustained. Apparent healing was obtained in only half of the cases when a cold abscess associated with cervical adenitis was treated by incision, drainage, and the injection of streptococcic enzymes, the procedure being covered by streptomycin in all but four cases. The period of follow-up is too short to be sure that we have secured permanent healing or to compare the results with those obtained for untreated patients. In the group treated for endobronchial disease associated with primary tuberculosis the response to therapy was never definite, and routine treatment of these patients has been abandoned.[14] The risk of emergence of bacilli resistant to streptomycin must be constantly borne in mind in deciding on the use of streptomycin in complications of tuberculosis for which its value is unproved.

This is particularly true in primary tuberculosis. But the most compelling reason for considering the use of streptomycin contraindicated in primary tuberculosis is the lack of evidence that streptomycin is effective. Those who are treating children for primary tuberculosis should publish their results and evaluate them in terms of their previous results with primary tuberculosis without specific treatment.

Many new drugs have been introduced as tuberculostatic agents. None approaches the value of streptomycin in the treatment of tuberculosis. A drug is needed which will surpass streptomycin in efficacy and which can be given safely for long periods without emergence of resistant organisms.

13. Lincoln, E. M., and Kirmse, T. W.: Streptomycin and Promizole in Miliary Tuberculosis and Tuberculous Meningitis in Children, Lancet **1**:767 (May 7) 1949.

14. Daly, J. F.; Brown, D. S.; Lincoln, E. M., and Wilking, V. N.: Endobronchial Tuberculosis in Children, to be published.

SUMMARY

The use of streptomycin is mandatory in meningitis, miliary tuberculosis, protracted forms of hematogenous tuberculosis, progressive primary tuberculosis with cavitation and bronchogenic spread, and progressive advanced chronic pulmonary tuberculosis. In meningitis it should be administered by both intrathecal and intramuscular routes in order to secure best results. A constant search for new methods of treatment must be made in order still further to improve the survival rate of meningitis. Intrathecal tuberculin seems to offer some help in this direction.

Streptomycin may be used as an elective measure in various nonfatal complications of tuberculosis, but its use should always be weighed carefully in each case in relation to expected response of the complication to other forms of treatment and to the possible future needs of the patient for streptomycin for other forms of tuberculosis.

The use of streptomycin should be considered contraindicated in uncomplicated, asymptomatic primary tuberculosis regardless of the age of the child or size of the primary complex, because it has not been shown to effect rapid cure of the primary form or to prevent complications and also because of the danger of the emergence of tubercle bacilli resistant to streptomycin, thus preventing effective use of the drug in the event of a serious complication.

Streptomycin should always be used in combined therapy if treatment is continued for more than three weeks.

ALLERGIC DERMAL-RESPIRATORY SYNDROME IN CHILDREN

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THE ALLERGIC dermal-respiratory syndrome may be defined as a symptom complex in which both dermal (urticaria, eczema) and respiratory (perennial rhinitis, hay fever, asthma) manifestations of allergy occur in the same patient, either synchronously or at different periods. It is the purpose of this paper to analyze a series of cases in children, first, to point out the importance of the dermal-respiratory syndrome by showing the frequency of its occurrence and, second, to indicate how the development of the respiratory aspects of the syndrome may be predicted and prevented or minimized by appropriate early treatment.

The data to be analyzed are from 750 cases seen in clinic and private practice over a number of years. The records were taken consecutively from the files, the only criteria being that the patient was allergic and had been completely studied. Complete studies include skin tests for foods as well as inhalant substances. Of these cases, 250 were analyzed previously from the standpoint of age of onset.[1a]

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1. (*a*) Ratner, B.: Allergy in Childhood: Its Onset and Natural Progress, J. A. M. A. **111**:2345 (Dec. 24) 1938. (*b*) Bray, G. W.: Asthmatic Child, Arch. Dis. Childhood **5**:237, 1930. (*c*) Thomson, J.: Clinical Study and Treatment of Sick Children, ed. 4, Edinburgh, Oliver and Boyd, 1925, p. 545. (*d*) Herman, H.: A Clinical Study of Sixty-One Cases of Asthma and Eczema in Infancy and Childhood Controlled by Cutaneous Protein Sensitization Tests, Am. J. Dis. Child. **24**:221 (Sept.) 1922. (*e*) Still, G. F.: Common Disorders and Diseases of Childhood, ed. 4, London, Oxford University Press, 1924, p. 381. (*f*) Peshkin, M. M.: Asthma in Children: Incidence and Significance of Eczema, Urticaria and Angioneurotic Edema, Am. J. Dis. Child. **32**:862 (Dec.) 1926. (*g*) Brock, J., and Hormes, M.: Statistische Untersuchungen über das kindliche Bronchialasthma (Zugleigh ein Beitrag zur Klimawirkung von Bad Dürrheim), Deutsche med. Wchnschr. **68**:1120, 1942. (*h*) Bullen, S. S.: Some Observations on Natural History of Asthma in Childhood, New York J. Med. **29**:545, 1929. (*i*) Edgren, G.: Prognose und Erblichkeitsmomente bei Ekzema infantum: eine klinisch-statistische Untersuchungen von Allergieerscheinungen, Acta paediat. (Supp. 2) **30**:1, 1943. (*j*) Moro, E., and Kolb, L.: Ueber das Schicksal von Ekzemkindern, Monatschr. Kinderh. **9**:428, 1910. (*k*) Peck, S. M., and Salomon, G.: Eczema of Infancy and Childhood: Contacts as Etiologic Agents, with Particular Reference to Feathers, Am. J. Dis. Child. **46**:1308 (Dec.) 1933. (*l*) O'Keefe, E. S., and Rackemann, F. M.: Studies in Asthma: Eczema: Its Relation to Allergy, J. A. M. A. **92**:883 (March 16) 1929. (*m*) Smyth, F. S.; Bain, K. M., and Stallings, M.: Infantile Eczema: Study Based on 160 Cases, ibid. **97**:1291 (Oct. 31) 1931. (*n*) Edwards, H. E.: Aspects of Perennial Allergic Rhinitis and Asthma in Childhood, Canad. M. A. J. **61**:36, 1949.

RESULTS

From Table 1 it will be noted that 15% of the patients were seen during infancy, a total of 41% before 5 years of age, and a total of 77% before 10 years of age. The series is comprised of 451 boys and 299 girls, or a ratio of boys to girls of 1.5 : 1.

Table 2 shows graphically the different symptom complexes into which the 750 cases fell. Thirty-five per cent of the total number falls into the dermal-respiratory category, which at once gives evidence of the significance of this syndrome in childhood allergy.

TABLE 1.—*Age at Which Patients Were First Seen*

	No. of Cases	%
Birth to 2 yr.	109	15
2 to 5 yr.	198	27
5 to 10 yr.	265	35
10 to 15 yr.	115	15
15 yr. and over	63	8
Total	750	100
Birth to 5 yr.	307	41
Birth to 10 yr.	572	77

TABLE 2.—*Distribution of Allergic Syndromes Among 750 Allergic Children*

	No. of Cases	%
Allergic dermal-respiratory syndrome	262	35
Respiratory syndromes without dermal manifestations	306	41
Dermal syndromes without respiratory manifestations	166	22
Other miscellaneous allergic syndromes	16	2

TABLE 3.—*Further Breakdown of the Dermal-Respiratory Syndrome in Relation to the Other Allergic Syndromes*

Allergic Manifestations	No. of Cases	%
Dermal-respiratory syndrome		
Eczema, asthma	88	11.6
Eczema, hay fever	12	1.6
Eczema, asthma, hay fever	23	3.1
Asthma, urticaria	31	4.1
Hay fever, urticaria	14	1.9
Asthma, hay fever, urticaria	18	2.4
Eczema, asthma, urticaria	32	4.3
Eczema, hay fever, urticaria	6	0.8
Eczema, asthma, hay fever, urticaria	14	1.9
Eczema, early upper respiratory tract allergy	10	1.3
Urticaria, early upper respiratory tract allergy	11	1.5
Eczema, urticaria, early upper respiratory tract allergy	3	0.4
Other allergic syndromes		
Asthma alone	181	24.2
Hay fever alone	52	6.9
Asthma and hay fever	40	5.4
Early upper respiratory tract allergy	33	4.4
Eczema alone	111	14.8
Urticaria alone	34	4.5
Eczema and urticaria	21	2.8
Miscellaneous	16	2.1
Total	750	100

In Table 3 we have made a further analysis of the cases charted in Table 2, according to the specific diagnosis in each case. Among the dermal-respiratory cases there is a greater preponderance of eczema in association with asthma than with hay fever. The figures also disclose the high incidence of both eczema and asthma as individual manifestations.

Table 4 reveals that in 59% of all the patients with eczema or with a history of eczema respiratory allergy developed.

From an examination of the data it would therefore appear that (1) in every third allergic patient the dermal-respiratory syndrome may be expected to develop and (2) in over one-half of all patients with eczema respiratory allergy develops.

TABLE 4.—*Relation of the Dermal-Respiratory Syndrome to Eczema*

Total No. of Cases	Total No. of Eczema Cases	Eczema Cases with Later Respiratory Allergy	
		No.	%
750	320	188	59

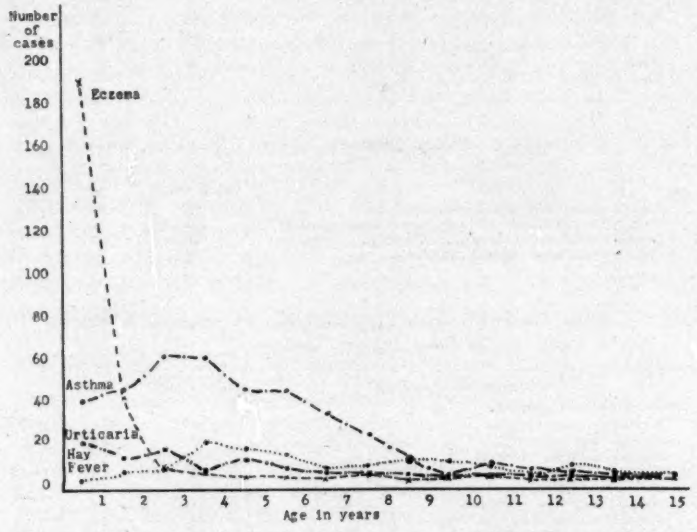

Fig. 1.—Age of onset of allergic syndromes; data included 265 cases of eczema, 367 of asthma, 117 of hay fever, and 96 of urticaria.

Table 5 shows the average age of onset for each of the four major allergic manifestations. The age of onset appears to be essentially the same whether the cases do or do not fall into the dermal-respiratory group. Hay fever is the exception, and the age at which it appears is significantly though slightly earlier in the dermal-respiratory group than in patients who suffer from hay fever alone.

TABLE 5.—*Average Age of Onset*

	Eczema	Urticaria		Asthma		Hay Fever	
	Mo.	Yr.	Mo.	Yr.	Mo.	Yr.	Mo.
In dermal-respiratory group.....	9½	4	7	4	4	5	6
Not in dermal-respiratory group.....	8½	4	8	4	1	7	9
All cases.....	9	4	7	4	2	6	9

In Figure 1 we have mapped the distribution curves for the age of onset for each of the four major allergic syndromes. There are several interesting observations to be made from it, especially if compared with a similar figure taken from an earlier paper in which the first 250 cases were analyzed.[1a] The chief difference is the rise in the hay fever curve in the earlier paper and the absence of any rise in the present series (Fig. 1). This may be attributed to the earlier diagnosis of hay fever in the last 500 cases because of the inclusion of intracutaneous pollen tests for the younger patients. The eczema curve confirms the generally accepted view that eczema in childhood always has its onset during the first year of life. The asthma curve reemphasizes what had already been pointed out,[1a] that childhood asthma generally makes its appearance by the 8th or 10th year, and in the bulk of cases it develops by 4 years of age. Hay fever usually occurs by the sixth or seventh year.

A word of explanation must be given for the fact that all the four curves approach the base line during the 14th year. This results from the fact that the patients under discussion are children, with the onset of allergic symptoms before the 15th birthday in all but 15 of the 750 cases. These 15 cases are not included in the age of onset chart.

COMMENT ON RESULTS

The data presented, showing that 35% of 750 unselected allergic patients belong to the allergic dermal-respiratory category, serve to emphasize the importance of this symptom complex. Actually the percentage may be higher, because many of the patients, particularly those with infantile eczema who were benefited by our treatment, were not followed long enough to rule out the subsequent development of respiratory allergy.

That eczema may be a precursor of other allergic manifestations is not a new observation. This has repeatedly been pointed out in the literature and supported by a large series of cases. A number of authors agree essentially with our figure of a 35% incidence. In 13 series of children presented by various authors [1b,a] in the United States, Canada, England, and Germany in which sufficient data were published for us to calculate the over-all percentage, we found that the incidence of cases with the dermal-respiratory syndrome averaged about 28%.

EVOLUTION OF THE DERMAL-RESPIRATORY SYNDROME

Before we consider the question of the types of allergic patients in whom the dermal-respiratory syndrome is prone to develop, we must point out that our observations indicate that there are three stages in the evolution of the fully developed dermal-respiratory syndrome, based upon clinical signs and skin-test findings. In the series forming the basis for this paper, 428 patients, or 44% of the 750 analyzed, presented dermal allergy alone or the fully developed dermal-respiratory syndrome. But of these, only 326 were tested adequately enough, we believe, to permit us to make the classification into the stages described in Table 6. Skin tests were performed during infancy in 52 cases and after the second birthday in 274.

In Stage I dermal allergy is present, but no respiratory symptoms have yet developed. Positive dermal reactions are obtained with foods but not with inhalants and pollens (Table 6, Fig. 2). In our series these cases comprised 7% of the total, of which 61% were infants. There is no way of telling whether a patient in

this stage will go on to a further stage. The child should be watched carefully for early evidence of respiratory allergy.

In Stage II there are two alternate phases, designated as IIA and IIB, which the course of development may assume. On the one hand (Stage IIA), the child has dermal allergy, a sensitivity to inhalants as determined by skin tests, but no manifest symptoms of respiratory allergy. On the other hand (Stage IIB), the child may present both dermal and respiratory symptoms, but the skin tests with inhalant substances give negative results.

In both IIA and IIB a higher percentage of children than infants is found, indicating that these stages have evolved from Stage I, and they comprise 31% of all the cases.

In Stage III both dermal and respiratory symptoms are present, and skin tests with pollens and/or inhalants show positive reactions. This is the fully developed dermal-respiratory syndrome. The majority of our patients, 62% of the 326 patients, came to us in this stage. Of this number, only 4% were infants.

TABLE 6.—*Stages in the Evolution of the Dermal-Respiratory Syndrome Analyzed in 326 of the 750 Allergic Children*

Stage of Evolution	Type of Syndrome	Inhalant Protein Skin Reactions	Total Cases		Distribution of Cases According to Age Group, %	
			No.	%	Infants *	Children
Stage I	Dermal allergy	Negative	23	7	61	39
Stage II, A	Dermal allergy	Positive	85	26	33	67
Stage II, B	Dermal-respiratory allergy	Negative	15	5	13	87
Stage III	Dermal-respiratory allergy	Positive	203	62	4	96

* Under 2 years of age when tested.

Table 6 and Fig. 2 show the evolution from uncomplicated dermal allergy, with negative skin reactions to pollens and inhalants, to the fully developed dermal-respiratory syndrome, with positive skin reactions to pollens and inhalants.

It is interesting to note that there is a preponderance of infants (61%) in Stage I and a mounting preponderance of children in Stages IIA and IIB that reaches an incidence of 96% in Stage III. This lends support to our concept of the evolutionary character of this symptom complex, indicating that dermal allergy predominates in infancy and gradually as exposure to pollens and inhalants increases new sensitivities and manifestations may develop. Stages IIA and IIB must be regarded as transitional. Patients in Stage IIA should be observed for evidences of new symptoms of respiratory allergy, and those in Stage IIB must be tested at intervals for evidence of new sensitivities, especially to pollens and inhalants.

From the evidence presented here it would seem highly probable that cases in Stages IIA or IIB will evolve into the third stage.

CERTAIN CASES EXEMPLIFYING THE EVOLUTION OF THIS SYNDROME

CASE 1.—This girl, S. F., first had eczema at 9 months of age. The skin cleared with local treatment, but symptoms recurred from time to time, remaining relatively mild. However, at 2 years of age, when she first was referred to us, the eczema was widespread and severe.

Tests at 2½ years revealed positive reactions to wool and cottonseed. This child was therefore in Stage IIA (Fig. 2). Little or no cooperation was given, and she was lost sight of for several years.

She returned six years later, when she was 9 years of age, with severe eczema localized to her neck, arms, and legs, and in addition she presented signs of hay fever. Three years prior she began to show signs of pollinosis, for which she was treated sporadically by various physicians. In other words, she was now in Stage III. At this time we found her sensitive to several pollens, several epidermal inhalants, and several molds. We then treated her for a period of about three years, and her eczema and hay fever were much improved. Treatment consisted of local therapy, immunization against the offending substances, and thyroid medication (because of retarded skeletal maturation).

Neither the patient nor the parents were cooperative, however. The patient again left us for a period of two years, and she returned with a marked exacerbation of her eczema and hay fever and early evidences of asthma. The eczema was somewhat abated, but the hay fever was severe. By now there was evidence of psychogenic difficulties. The girl was now 14 years of age. We advised therapy, but without cooperation poor results were obtained, and after an inconclusive period she again left us.

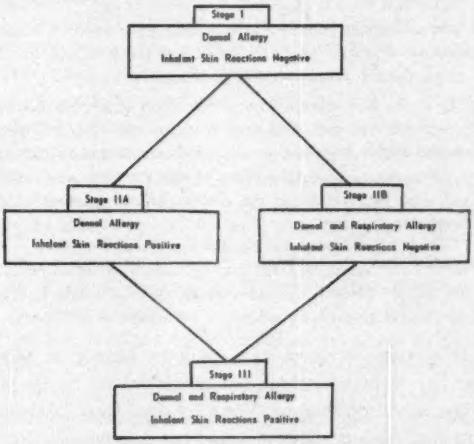

Fig. 2.—Stages of the dermal-respiratory syndrome.

This case is an example of an instance in which the whole gamut of the syndrome is evolved, starting with infantile eczema and finally becoming an intractable dermal-respiratory case with great psychological trauma.

One cannot say with assurance that the hay fever could have been aborted or minimized in this case with consistent immunization therapy. One can at least state that no real cooperation was given by the patient and parents, and we would like to attribute our failure at least in part to this factor.

It perhaps will be more profitable to present some cases in which appropriate treatment apparently did prevent the development of the respiratory phase.

CASE 2.—In this patient, a girl, B. F., eczema developed at 6 months of age and rapidly became generalized. She also had two attacks of hives during infancy. The child was first seen at 2 years of age, when a severe generalized eczema was still present.

Positive scratch reactions were obtained with a number of foods and with indigenous environmental substances containing cotton, wool, dust, feathers, and kapok. Positive intradermal reactions were obtained with ragweed and bacteria, inhalant mixture, and trees. The patient had at this time presented no respiratory symptoms (Stage IIA).

She was treated consistently for three years with local therapy, elimination of the offending foods, and immunizations against bacteria and inhalants. Roentgenograms of the wrists showed a skeletal retardation, and she was given thyroid medication throughout this period. Her eczema cleared after about six months and has never recurred.

At 5 years of age the protein skin testing was repeated, and additional positive reactions were obtained with pollens and molds. The immunization therapy was therefore broadened to include these newly acquired sensitivities.

Although the nasal smear contained large numbers of eosinophiles during the summer and fall, the patient at 7 years of age had only very mild clinical respiratory symptoms, consisting of a mucoid nasal discharge and mild sneezing, but no asthma or hay fever has developed. The child is still under treatment at 9 years of age.

CASE 3.—In patient J. B. eczema first appeared at 9 months of age, and he also had several attacks of hives during infancy. He was first seen at 21 months of age, when the eczema was generalized. Scratch tests showed positive reactions to several foods, ragweed, and several indigenous environmental samples, including wool and house dust (Stage IIA). Regular treatment was instituted. The skin became clear before 3 years of age. At 3 years of age the skin tests were repeated, and additional pollens and inhalants gave positive reactions. These were added to the immunization schedule. At 7 years of age there is still no clinical evidence of respiratory allergy. The patient remains under treatment.

CASE 4.—Patient J. B. W. had eczema from birth which gradually became generalized and increased in severity until he was first seen at 4 years of age. Scratch tests showed positive reactions to orris root and rabbit hair, and an intracutaneous test with ragweed gave a positive reaction. Treatment was outlined, and at 5 years of age the skin was clear. Hives appeared occasionally, and there were recurrences of the eczema, but these were of brief duration. At 8 years of age the intracutaneous tests were repeated and additional positive reactions obtained with several molds. These were added to the desensitization injections. At 9 years of age the intracutaneous tests were again repeated and additional positive reactions obtained with cocklebur, grasses, and trees. These were added to the desensitization injections. At 10 years of age he still has no clinical respiratory allergy. Treatment is still being given.

What the final outcome of these cases will be cannot be predicted, but it is interesting that no hay fever or asthma has developed up to the present time with the institution of immunization therapy. We have cited them because we believe they fortify our concept that eczema patients who give positive reactions to pollens and other inhalants should be treated as potential hay fever and asthma patients.

Every effort should be made to institute treatment even though no respiratory symptoms have as yet developed. Tests should be repeated to detect the development of new sensitivities. Treatment should be carried on over a period of years. It is hoped that this procedure will abort the full-blown dermal-respiratory syndrome such as was noted in Case 1 and will eventually lead to fewer cases continuing into adult life.

MANAGEMENT

In the first place, the patient with dermal allergy should be completely tested with all available proteins, including indigenous environmental samples, and not just with foods, as is sometimes done in infantile eczema.

In general terms the investigation and treatment of each of the four stages of the dermal-respiratory syndrome are the same. The patient is carefully appraised by physical examination, urinalysis, cytological blood studies, capillary microscopy of the nailfold, and fluoroscopy and/or roentgenography of the hand and wrist bones, heart, lungs, and sinuses.

At the beginning of the allergic investigation the patient is put on a denatured diet in which all protein-containing foods are thoroughly cooked.[2] The patient is then completely tested by the scratch and intracutaneous methods with all available proteins and with indigenous environmental samples.

Meanwhile, the dermal lesions are treated symptomatically to alleviate the itching and heal the damaged epidermis. Local treatment includes such preparations as lotions and dyes for the wet stage and ointments for the dry stage. Thyroid is administered if indicated, by the finding of a delay in bone maturation, and unsaturated fatty acids (such as corn oil, soya bean oil, lard) are given by mouth.

Evidence for the presence of respiratory allergy is sought by history, physical examination, and repeated nasal smears. If respiratory allergy is not present when the patient is first seen, repeated observations are made frequently so that it will be detected as soon as it appears.

As soon as the testing has been completed, treatment is started by removing all the foods causing a positive reaction from the diet, correcting the environment, and immunizing the patient by subcutaneous injections with all the inhalant and pollen allergens to which he gave positive reactions.

If positive reactions with inhalants and pollens are obtained at the initial testing, these substances should preferably be included in the treatment of the skin disease, and in this way future manifestations of respiratory allergy may be aborted or reduced in severity. If positive reactions to inhalants and pollens are not obtained at the initial studies, the tests should be repeated at yearly intervals, particularly if the skin manifestations do not respond to treatment properly and/or allergic respiratory manifestations are beginning to be shown. In this way, newly developed sensitivities can be detected and proper treatment instituted before pronounced manifestations of hay fever or asthma appear.

The fact that we see patients with dermatitis in whom positive reactions are obtained with pollens and inhalants but in whom respiratory allergy does not develop, as shown by retesting, does not invalidate our hypothesis in any way. In the first place, pollens and inhalants are important in the etiology of many cases of allergic dermatitis, and they should therefore be included in treatment of the dermatitis just as much as should the elimination of foods causing positive reactions and the local treatment of the rash, in spite of the fact that pollens and inhalants are more generally associated with respiratory manifestations. The fact that in many such patients (59%) respiratory symptoms later develop would indicate that desensitization procedures with the pollens and inhalants causing positive reactions are more logical than mere hoping that the patient will "grow out of his allergy" and escape further disability.

Moreover, all patients with dermal allergy should be carefully observed for mild forms of respiratory allergy. Repeated "colds" should be regarded as allergic rhinitis until proved otherwise. The best means of studying these is by the nasal smear developed by Hansel.[3] Repeated smears are necessary, as attacks of allergic rhinitis may be interspersed with true nasal infections. The allergic rhinitis may escape

2. Ratner, B.: Treatment of Milk Allergy and Its Basic Principles, J. A. M. A. **105**:934 (Sept. 21); 1935. Round Table Discussion on Food Allergy in Children, J. Pediat. **16**:653, 1940.

3. Hansel, F. K.: Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Company, 1936.

diagnosis unless the nasal smears are taken at the proper time. Chronic nasal congestion, chronic cough, and repeated bouts of pneumonia should likewise be suspect if they occur in patients with dermal allergy.

Another method of attack in preventing respiratory allergies from developing in patients with dermal allergy is the correction of the patient's environment so that inhalant substances to which the patient may become sensitive are kept to a minimum. For example, such common allergens as house dust, feathers, and cotton linters should be excluded from the patient's environment so far as possible.

COMMENT

We are here concerned with a phenomenon which is generally recognized by those interested in allergy. Those acquainted with the developments in pediatric allergy would therefore ask, "What is there new about the dermal-respiratory syndrome with which we are not already familiar?"

Since Elliotson,[4] in 1831, described the first case of pollen dermatitis and Blackley,[5] in 1873, reported the first experimental observation of pollen dermatitis, it has been repeatedly shown by many authors[6] that inhalants and pollens are frequently of considerable importance in the causation of allergic dermatitis, including infantile eczema.

As recently as 1950, Tuft and co-workers[7] reemphasized the importance of inhalants in the etiology of atopic dermatitis and report an investigation of a 29-year-old man with eczema. The dermal symptoms were reproduced repeatedly by controlled exposure to the inhalant allergens in this instance, house dust and Alternaria. Although some foods gave positive intradermal reactions, these foods were found to be unimportant in the causation of the dermatitis. They claim that this is the first case in which the specific lesions of atopic dermatitis were induced repeatedly by

4. Elliotson, J.: Hay Fever, Lancet **2**:370, 1830-1831.

5. Blackley, C. H.: Experimental Researches on the Causes and Nature of Catarrhus Aestivus (Hay Fever or Hay-Asthma), London, Baillere, Tindall and Cox, 1873.

6. (*a*) Walker, C.: Causation of Eczema, Urticaria and Angioneurotic Edema by Proteins Other than Those Derived from Food, J. A. M. A. **70**:897 (March 30) 1918. (*b*) Hill, L. W.: Sensitivity to Environmental Allergens in Infantile Eczema: Role of Specific Allergens, New England J. Med. **213**:135, 1935. (*c*) Sensitivity to House Dust and Goose Feathers in Infantile Eczema, J. Allergy **9**:37, 1937. (*d*) Osborne, E. D., and Walker, H. L.: Contact and Environmental Allergens as a Cause of Eczema in Infants and in Children, Arch. Dermat. & Syph. **38**: 511 (Oct.) 1938. (*e*) Netherton, E. W.: Atopic Dermatitis, M. Clin. North America **22**:333, 1938. (*f*) Feinberg, S. M.: Seasonal Atopic Dermatitis: Role of Inhalant Atopens, Arch. Dermat. & Syph. **40**:200 (Aug.) 1939. (*g*) Rowe, A. H.: Dermatitis of the Hands Due to Atopic Allergy to Pollen, ibid. **53**:437 (May) 1946. (*h*) Simon, F. A.: Atopic Dermatitis in Infants, Children and Adults, with Special Reference to the Role of Inhalants and Dander, J. Allergy **18**:186, 1947. (*i*) Tuft, L.: Importance of Inhalant Allergens in Atopic Dermatitis, J. Invest. Dermat. **12**:211, 1949. (*j*) Figley, K. D., and Parkhurst, H. J.: Silk Sensitivity: With Especial Reference to Its Rôle in Atopic Eczema, J. Allergy **5**:60, 1933. (*k*) Hill, L. W.: Atopic Dermatitis, Am. J. Dis. Child. **76**:583 (Nov.) 1948. (*l*) O'Keefe, E. S.: Analysis of 300 Cases of Asthma in Children, New England J. Med. **214**:62, 1936. (*m*) Sulzberger, M. B., and Vaughan, W. T.: Experiments in Silk Hypersensitivity and Inhalation of Allergen in Atopic Dermatitis (Neurodermatitis Disseminatus), J. Allergy **5**:554, 1934. (*n*) Taub, S. J.: Allergy Due to Silk, ibid. **1**:539, 1930. (*o*) Peck and Salomon.[1k]

7. Tuft, L.; Tuft, H. S., and Heck, V. M.: Atopic Dermatitis: Experimental Clinical Study of the Role of Inhalant Allergens, J. Allergy **21**:181, 1950.

deliberate exposure of the patient to the offending inhalant. Figley and Parkhurst,[6j] in 1933, and Sulzberger and Vaughan,[6m] in 1934, reported interesting observations on cases of silk sensitivity that resulted in dermal and respiratory symptoms from inhalation of the antigen.

It might be argued that there is no real justification for attempting to create or coin a new name for this complex, for Peshkin [1f] in 1926 stated that patients with eczema shown to be sensitive to a biologic food group should be tested further with pollen and inhalant proteins, that many of these patients would show sensitization to the latter proteins, and that the elimination of such sensitizing substances might prevent the onset of asthma. This is our thesis essentially, but we have chosen to designate it as the dermal-respiratory syndrome, perhaps more for emphasis and orientation than to describe a new clinical concept.

Stuart and Farnham,[8] in the same year as Peshkin, showed rather interestingly that as children get older, they tend to lose their food sensitivities and acquire inhalant sensitivities, and they suggested that it would be advisable for asthmatic children to avoid unnecessary contact with inhalant substances, even if they show negative skin reactions, because of the danger of the development of new sensitivities.

Bray,[1b] as early as 1930, also called attention to this phenomenon and stated that bronchitic attacks in children with eczema and prurigo should be regarded as potential asthma, and coughs, sneezing, and coryza should be quickly investigated.

In 1933 Peck and Salomon,[1k] who were chiefly concerned with the dermatitis phase of this syndrome, found that a large number of their infantile eczema patients reacted to feather proteins and other inhalants, and they voiced the opinion that eczema in infancy was perhaps oftener related to contactants than to foods.

Hill,[6b] in 1935, pointed out the changing attitude in relation to the causative allergens in eczema. He found that the animal epidermals and other environmental allergens, as well as foods, must be taken into consideration in the search for the etiologic factor in eczema in children. Their significance may not be great in the first year of life, but in the second year they are as important as food.

Glaser [9] and Ratner [10] both suggested that the treatment of eczema should include the outlining of a way of life that would prevent the development of more serious allergic manifestations, such as asthma.

More recently Ross and Brown [11] found that in some instances if an allergic child who previously had negative skin reactions to inhalants was given repeated exposures to such inhalants as animal danders and feathers, he would show positive skin reactions to these inhalants with associated attacks of asthma. They urged that exposure to these allergens be kept to a minimum in order to minimize or prevent the respiratory manifestations.

The evidence presented here we hope will leave little doubt about the validity of the dermal-respiratory syndrome. We have carefully analyzed the records of 750 allergic patients to study the evolution of this syndrome. That 35% in our series

8. Stuart, H. C., and Farnham, M.: Acquisition and Loss of Hypersensitiveness in Early Life, Am. J. Dis. Child. **32**:341 (Sept.) 1926.

9. Glaser, J.: Treatment of Eczema (Atopic Dermatitis) in Infancy, J. A. M. A. **137**:527 (June 5) 1948.

10. Ratner, B.: Pediatric Approach to the Management of Allergic Eczema in Children, New York J. Med. **48**:296, 1948.

11. Ross, J. R., and Brown, A.: Management of Atopic Eczema Cases in Infancy and Childhood, Canad. M. A. J. **58**:486, 1948.

proved to belong in this category gives evidence of the relative importance of this allergic phenomenon. The patients with infantile eczema which was unusually severe in character and persisted for more than a year were those in whom eventually respiratory symptoms developed. The problem therefore becomes a challenge in every case of eczema.

The fact that in so many infants and children with dermal allergy respiratory symptoms later develop shows that the importance of the relation between dermal and respiratory allergy is not sufficiently appreciated. Every case of dermal allergy should be regarded as a potential case of asthma or hay fever. Once this is realized, there are many ways in which developing respiratory allergies may be detected and prevented or minimized.

Eczema in infancy and childhood should not be regarded solely as a dermatologic condition. It should be treated from a broad general and allergic standpoint, and treatment should include outlining a way of life for the patient which will prevent the development of more serious allergic manifestations, such as asthma.

CONCLUSIONS

The allergic dermal-respiratory syndrome may be defined as a symptom complex in which both dermal and respiratory manifestations of allergy occur in the same patient, either synchronously or at different periods.

Thirty-five per cent of allergic children, or every third allergic child, falls into this category, which gives evidence of the significance of this syndrome in childhood allergy.

Fifty-nine per cent, or approximately every second child, with allergic eczema or with a history of eczema later has respiratory allergy.

Among the dermal-respiratory cases, a greater number present eczema in association with asthma than with hay fever.

The generally accepted view that eczema in childhood almost always has its onset in infancy; chiefly during the first year, is confirmed.

Our present findings with respect to the age of onset for asthma reaffirms our previous observation that if asthma is to appear during childhood, it has nearly always made its appearance by the eighth year, and in the majority of cases asthma appears by 4 years of age.

Hay fever usually dates its onset before the seventh year.

The various phases of the dermal-respiratory syndrome follow a similar age of onset pattern.

Three stages in the evolution of this syndrome are described: Stage I: dermal manifestations, absence of respiratory symptoms, negative skin reactions to inhalants, present chiefly in infants; Stage IIA: dermal manifestations, no respiratory symptoms, positive skin reactions to inhalants; Stage IIB: dermal and respiratory manifestations, negative skin reactions to inhalants; Stage III: dermal and respiratory symptoms, positive skin reactions to inhalants, occurs almost entirely in older children.

Eczema in infancy and childhood should not be regarded solely as a dermatologic condition. Every case of dermal allergy should be viewed as a potential case of asthma or hay fever. The need for adequate and appropriate treatment for inhalant sensitivity is stressed.

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INFANT FEEDING WITH AND WITHOUT ADDED CARBOHYDRATE

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THE PURPOSE of this paper is to present comparative experiences in the use of formulas with and without added carbohydrate for infant feeding. The use of formulas without added carbohydrate has been reported by others.[1] However, comparative data for periods longer than the newborn period have not been presented.

Approximately 98% of the infants born in the city of Rochester, Minn., are delivered in one hospital and are under the care of the pediatric service throughout the newborn period. During the past three and one-half years formulas without added carbohydrate have been used when infants were not breast fed and when preference for some other particular feeding was not expressed by the mother. Prior to that time formulas with added carbohydrate were used routinely.

The infants herein considered were chosen in sequence of birth dates from those born during the periods of Aug. 1, 1946, through July 31, 1947, and Sept. 1, 1947, through Sept. 30, 1948. The group of infants receiving formulas with added carbohydrate consisted of those whose birth date was within the first period, and the group of infants receiving formulas without added carbohydrate consisted of those whose birth date was within the second period. Ninety-five per cent of the infants born in Rochester are registered in the well-child clinics, and approximately 75 to 80% of the infants registered are seen six times or more during the first year. The infants included in this study are those who received one particular type of feeding continuously for the first six months of life. The formulas prescribed for these infants were prepared by using fresh or evaporated cow's milk and water, with or without added carbohydrate. Infants who were breast fed for six months or more were included for comparison of gains in weight.

From the Section on Pediatrics, Mayo Clinic, and the Rochester Child Health Institute.

Read at the meeting of the Illinois State Medical Society, Chicago, May 22, 1951. (Released by the secretary of the society for publication.)

1. (*a*) Adams, J. H.: A Simple Formula for Premature and Full Term Infants, J. Pediat. **33**:23-28 (July) 1948. (*b*) McMahon, H. O.: A Simplified Infant Feeding Formula: A Report of the Use of Irradiated Evaporated Milk and Water in 2,004 Cases, Wisconsin M. J. **38**:874-876 (Oct.) 1939. (*c*) McCulloch, H.: Use of Evaporated Milk Without Added Sugar for the Feeding of Infants, Am. J. Dis. Child. **67**:52-55 (Jan.) 1944. (*d*) Litchfield, H. R.: Evaporated Milk in Infant Feeding: An Evaluation With and Without Added Carbohydrate, Arch. Pediat. **61**:617-625 (Dec.) 1944. (*e*) The Department of Pediatrics of University of Chicago: Liberal Infant Feeding, J. Am. Dietet. A. **22**:602-604 (July) 1946.

Infants in the following three categories were not included in this study: (1) infants whose birth weight was less than 5 lb. (2,300 gm.), (2) infants who were seen less than six times in the well-child clinics during the first year of life, and (3) those infants classed as receiving mixed feeding during the first six months of life. Approximately 70% of Category 3 were infants who were breast fed for less than six months. Some were infants fed with various proprietary milk preparations. Others were infants for whom the type of feeding was changed during the first six months for convenience or other reasons not associated with the formula being used. Eight infants in Category 3 were excluded from this study because at some time during the first six months of life the original formula prescribed was changed to another type of feeding. Recurrent loose stools occasioned the change of formula for all of these infants. The original feeding offered to four of this group was formula with added carbohydrate, and for the other four infants the original feeding was formula without added carbohydrate.

The youngest infant that was included in this study is now a child 2½ years of age, and the majority of the infants have been seen regularly in the well-child clinics since birth. They are from families that are representative of all economic levels in the city of Rochester. Nutritional disturbances, such as rickets, scurvy, and anemia, have not been noted in any of these infants. The average weights and heights of infants visiting the well-child clinics at the age of one year have remained essentially constant from 1946 through 1950.

It should be emphasized that all mothers were instructed in the "self-regulation" of infant feeding. In our experience self-regulation in regard to interval of feeding is quite successful in the majority of instances. However, there are some lethargic or small infants for whom a definite schedule of awakening for feeding may be indicated during the first several weeks. There are some mothers who gain self-confidence from a definite schedule. There are a few who operate a highly organized household and find it desirable to fit the time for feeding the infant into this schedule. Problems have not occurred, however, with self-regulation in regard to amounts of formula desired by the infant. Mothers have not been concerned about offering an infant as much formula as he or she desires. Occasionally the amount of formula offered may be limited because of misunderstanding.

Breast feeding is encouraged, and during the past five years approximately 60% of the infants received breast feeding without supplemental formula at the time the mother and infant were dismissed from the hospital. Dismissal from the hospital is usually on the seventh postpartum day. When feeding is artificial, the above formulas have been first offered to the infant late in the third day of life. In general, the same formula is used from the newborn period until the time when fresh whole unboiled milk is offered. The practice is to suggest the use of unboiled whole milk sometime between the 7th and 12th months of life, depending on circumstances of milk supply, mother's wishes, and instances of contemplated travel.

Mothers who are unable or do not wish to breast feed their babies are asked what formula they prefer, and their preference is adhered to so far as possible. If no specific desire is expressed, evaporated-milk formula is suggested.

FORMULAS USED

The formulas used for infant feeding in this study were the following:

Evaporated milk with added carbohydrate:	
Evaporated milk	1 part
Water	2 parts
Carbohydrate *	5 to 8%
Evaporated milk without added carbohydrate:	
Evaporated milk	2 parts
Water	3 parts
Fresh whole cow's milk with added carbohydrate:	
Milk	2 parts
Water	1 part
Carbohydrate *	5 to 8%
Fresh whole cow's milk without added carbohydrate:	
Milk	3 parts
Water	1 part

* Corn syrup or a dextrin-maltose preparation.

INSTRUCTIONS TO MOTHERS FOR FORMULA PREPARATION

Group instruction in general infant care is given at some time during the mother's lying-in period. Included are instructions for making either evaporated-milk or fresh-milk formulas and for use of some of the proprietary milk preparations. Mothers who are breast feeding receive these instructions also but in addition are advised in regard to lactation diet by a nutritionist.

Two simple methods are given for preparation of evaporated-milk formula. No particular brand of evaporated milk is recommended. The usual technic for sterilization of bottles and utensils is described. It is suggested that a teakettleful of water be put on the stove and boiled while the bottles are being sterilized. In both methods the top of the can of milk is cleansed with soap and water and then scalded with boiling water from the teakettle. Two holes are then punched in the top of the can in the usual manner. One method suggested is to empty the contents of one large can of evaporated milk (13 oz. [380 ml.]) into a sterile quart container and add sufficient boiled water (19 oz. [560 ml.]) to make 1 qt. (1,000 ml.). This dilution is nearly equivalent to 2 parts of evaporated milk and 3 parts of water. The use of the entire contents of a can of milk avoids the necessity of storing partially emptied cans. The formula is then transferred into bottles, the number of bottles and the amount in each being determined by the requirements of the particular infant. A second method is to make the mixture directly in sterilized bottles. The can of milk is prepared as described above and the estimated amount of milk poured into each bottle. Sufficient boiled water is then added from the teakettle. For example, if one wishes to prepare feedings consisting of 5 oz. of formula, the milk is poured up to the 2-oz. (60-ml.) mark on the bottle, and then boiled water is added to the 5-oz. mark. If one wishes to prepare feedings consisting of 8 oz. (240 ml.), evaporated milk is poured to the 3¼-oz. or 3½-oz. (96-ml. or 106-ml.) level, and sufficient water is added to make 8 oz. The bottles are then capped and refrigerated until used. Single bottles may be prepared for supplemental feedings by using the small (4-oz. [120-ml.]) can of evaporated milk. One or several bottles of sterile water may be prepared and capped and evaporated milk added from one of the small cans immediately before feeding. In these circumstances unused evaporated milk should be discarded. This method of formula preparation is especially convenient when one is traveling with an infant or if facilities are not available for refrigeration of prepared formula.

Ordinary or homogenized dairy milk is suggested for fresh-milk formulas. When a family's milk supply is from its own cows, a mixture of the milk from several cows is recommended. In this way daily fluctuation of butterfat content is minimized. If the content of butterfat is likely to be high, as in milk from Jersey cows, about one-third of the cream should be removed before the formula is prepared. The formula consists of 3 parts of milk and 1 part of water. The total amount of formula prepared will depend upon how much is necessary to meet the infant's needs for one day. Usually 24 oz. (710 ml.) of milk and 8 oz. of water will be sufficient. A measuring cup which has been sterilized with the bottles may be used. Milk and water are measured directly into a saucepan. The mixture is brought to a boil (not in a double boiler) and then allowed to simmer for 5 to 10 minutes. Approximately 2 oz. of water will be lost by evaporation and need not be replaced. The point is stressed that boiling is not only for sterilization but also for the purpose of producing a finer, more easily digested curd. The formula should be poured into the bottles through a small sterile tea strainer to remove coagulum which is produced by boiling and which may clog the nipple holes.

TABLE 1.—*Average Gains in Weight Under Different Feeding Conditions During the First Six Months of Life*

	Type of Feeding									
	Artificial									
	Without Added Carbohydrate				With Added Carbohydrate					
	Whole-Milk Formula		Evaporated-Milk Formula		Whole-Milk Formula		Evaporated-Milk Formula		Breast	
Month of Life	No.	Average Gain, Oz.	No.	Average Gain, Oz.	No.	Average Gain, Oz.	No.	Average Gain, Oz.	No.	Average Gain, Oz.
1	16	27.1	87	26.7	34	27.2	96	26.3	61	33.1
2	16	33.6	86	34.2	33	33.0	91	35.6	60	32.5
3	14	28.9	86	30.7	30	31.4	89	30.0	62	23.4
4	15	27.3	81	27.3	31	30.4	86	25.6	59	21.7
5	14	24.8	78	23.7	30	22.1	84	22.2	55	19.6
6	13	26.5	70	22.7	29	20.1	82	20.3	57	16.7
Total average gain		168.2		165.3		164.2		160.0		147.0

ADDITION OF OTHER FOODS

The administration of vitamins A, D, and C was recommended when the infants were one month of age. Some were given strained orange juice and a preparation containing vitamins A and D; others were given one of the water-soluble multiple vitamin preparations.

The practice in the well-child clinics has been to suggest the introduction of cereal in the diet when the infants attain the age of about 3 months. If the mother felt that the infant was not satisfied with formula alone, cereal was offered earlier. Strained vegetables and fruits were offered at about 4 months of age, egg yolk at 5 months, and strained meats at 6 months. The practices in regard to addition of these foods were the same throughout the time of this study.

EVALUATION OF GAINS IN WEIGHT WITH DIFFERENT TYPES OF FEEDING

The mean gains in ounces each month for the first six months of life are presented in Table 1. A group of infants who were entirely breast fed for at least six months is included for comparison. Gains each month were calculated for only the first six months of life. Since most of these infants were fed pasteurized whole cow's milk beginning at the seventh, eighth, or ninth month of age, the diets in

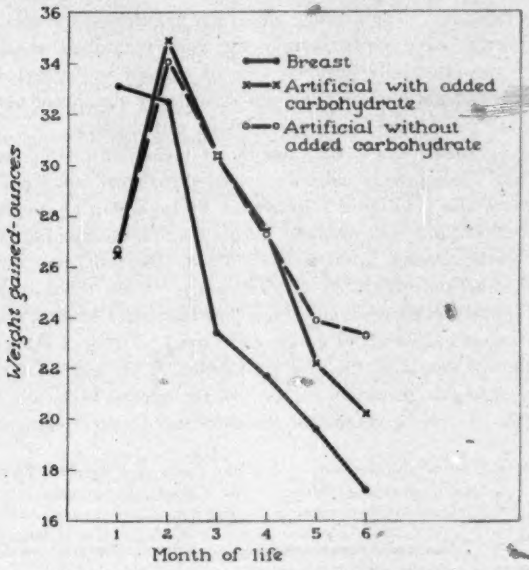

Fig. 1.—Average gain in weight each month.

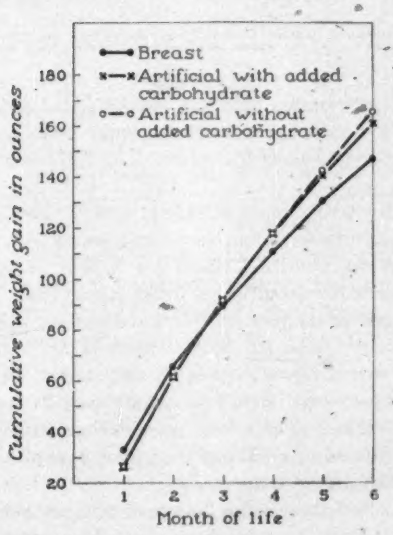

Fig. 2.—Average cumulative gains in weight.

respect to milk tended to be similar after the age of 7 months and, therefore, not amenable to comparison. The average gain each month and the total gain during the first six months were approximately the same regardless of whether fresh-whole-milk or evaporated-milk formulas with or without added carbohydrate were used. There was a slightly greater but not statistically significant average gain in weight by infants given formulas without added carbohydrate.

The average gains in weight each month for breast-fed infants and for infants receiving artificial feeding with and without added carbohydrate are shown graphically in Figures 1 and 2. Figure 1 shows the average gain in weight for each of the first six months of life. For example, during the first month of life the breast-fed infant gained, on the average, approximately 33 oz. (940 gm.), while the artificially fed infant gained approximately 26 oz. (740 gm.). In the third month of life the artificially fed infant gained, on the average, approximately 30 oz. (850 gm.), while the breast-fed infant gained about 23 oz. (650 gm.). Figure 2 shows the average cumulative gains in weight of the first six months of life and was constructed by totaling the average gain in weight for each of the months up to and including the indicated month. It will be noted that the patterns of gain in weight each month

TABLE 2.—*Average Amounts of Various Types of Formula Offered Each Twenty-Four Hours at the Age of Two Months*

Type of Formula Offered	Infants *	Average Amount Offered, Oz.
Fresh whole milk with added carbohydrate	36	39
Fresh whole milk without added carbohydrate	11	36
Evaporated milk with added carbohydrate	116	35
Evaporated milk without added carbohydrate	84	34

* The number in each category represents the infants who visited the well-child clinics at the age of 2 months whether or not they visited the clinics at all of the other monthly intervals during the first six months of life.

for the infants receiving formulas with and without added carbohydrate are almost identical. The pattern of gain in the breast-fed infant as shown in Figures 1 and 2 differs from that of the artificially fed infant. This difference in pattern has been shown by others.[2]

Do infants who are taking formula without added carbohydrate desire greater amounts in each 24 hours than do those receiving formula with added carbohydrate? During each visit in the well-child clinics the mother is asked to estimate the average amount of formula offered to her infant in one day. This information has been gathered routinely for the past five years and was not obtained specifically for this study. The amounts reported by the mothers are obviously not accurate measurements of the actual amounts taken by the infants. The average number of ounces of formula reported as offered to infants each 24 hours at the age of 2 months is shown in Table 2. There were no significant differences in the average amounts of formula offered to infants at the age of 2 months when formulas with or without added carbohydrate were used.

Is it necessary to offer cereal earlier to infants who are taking formulas without added carbohydrate? Data on the infants for whom early cereal feeding was

2. Faber, H. K., and Sutton, T. L.: Statistical Comparison of Breast-Fed and Bottle-Fed Babies During the First Year, with Special Reference to Gain in Weight and to Morbidity. Am. J. Dis. Child. **40**:1163-1176 (Dec.) 1930.

suggested are given in Table 3. The frequency with which cereal was suggested before the age of 3 months apparently did not depend upon whether or not the formula contained added carbohydrate.

May one expect difficulties in regard to firm or hard stools when formulas without added carbohydrate are used? Data on this point are given in Table 4. These data are based on the mother's statement at each clinic visit. The frequency with which firm to hard stools were reported in the group taking formula with added carbohydrate was 25%. In the group taking formula without carbohydrate the frequency was 14%. The frequency with which occasionally hard stools were reported was 13.5% when the formula offered contained added carbohydrate and 2.6% when the formula without added carbohydrate was taken. It was somewhat surprising to find that less difficulty with firm to hard stools was reported for the

TABLE 3.—*Relation of Early Cereal Feeding and Type of Formula Offered*

Type of Formula Offered	Total Infants *	Infants Offered Cereal Before Age of 3 Mo.	
		No.	%
Formula with added carbohydrate	148	44	29.7
Formula without added carbohydrate	114	32	28.1

* The number in each category represents the infants who came frequently enough in the first six months of life to yield adequate information in regard to the points covered in the table.

TABLE 4.—*Character of Stools During First Six Months of Life*

Type of Formula Offered	Total Infants*	Character of Stools									
		Soft	Occasionally Loose		Occasionally Firm		Occasionally Hard		Frequency of Firm to Hard Stools	
			No.	%	No.	%	No.	%	No.	%
Formula with added carbohydrate	148	105	6	4.1	17	11.5	20	13.5	37	25.0
Formula without added carbohydrate	114	95	3	2.6	13	11.4	3	2.6	16	14.0

* The number in each category represents the infants who came frequently enough in the first six months of life to yield adequate information in regard to the points covered in the table.

group receiving no added carbohydrate. Perhaps instruction to mothers has improved, thus enabling them to evaluate consistency and frequency of stools with greater appreciation of the limits of normal variation. At any rate, there were but two instances in which persistently hard stools were reported.

Infants occasionally have loose stools and excoriated buttocks when given evaporated-milk formulas during the newborn period. In some instances excoriation of the buttocks may occur without loose stools. In our experience the addition or omission of carbohydrate in the formula has had no effect. The loose stools and excoriated buttocks usually clear up rapidly when the formula is changed to a mixture containing boiled whole cow's milk. Evaporated milk may again be used in two or three weeks without difficulty. McCulloch [16] mentioned the possibility that the loose stools might be due to some alteration of the milk during the evaporation process. In his experience this occasional difficulty was apparently obviated by omitting carbohydrate.

Table 5 presents the incidence of "colic" in the two groups. I shall not attempt to discuss "colic" or to define it in any but a negative manner, as "that excessive crying for which no remediable reason was found." The designation as severe, mild, or possible is based primarily on persistence and severity of crying. The incidence of colic, and especially severe colic, was less in the group who received formulas without added carbohydrate, but other factors which may have contributed to the presence of colic have not been analyzed sufficiently to enable one to state with confidence that the frequency of colic in these two groups was related to the type of feeding.

COMMENT

It should be pointed out that formulas without added carbohydrate are not formulas without carbohydrate. Evidence presented by Litchfield [1d] for the necessity of carbohydrate in infant feeding would not seem to be apropos to a study comparing the use of formulas with and without added carbohydrate.

TABLE 5.—*Relation of Occurrence of "Colic" to Type of Formula Offered*

Type of Formula Offered	Total Infants*	Occurrence of "Colic"							
		Severe		Mild		Possible		Total	
		No.	%	No.	%	No.	%	No.	%
Formula with added carbohydrate....	148	10	6.8	16	10.8	3	2.0	29	19.6
Formula without added carbohydrate.	114	3	2.6	2	1.8	11	9.6	16	14.0

* The number in each category represents the infants who came frequently enough in the first six months of life to yield adequate information in regard to the points covered in the table.

Mothers included in the present study have not expressed apprehension in regard to this type of feeding, as has been reported by Adams.[1a] To the contrary, the remark is often made, "My, this is certainly easier than the way we did it before."

SUMMARY AND CONCLUSIONS

This paper presents comparative experiences in the use of formulas with and without added carbohydrate for infant feeding. Average gains in weight were essentially the same for infants taking formulas without added carbohydrate as for infants taking formulas with added carbohydrate.

The amount of formula offered to infants 2 months of age, as reported by the mother, was essentially the same for formulas without added carbohydrate as for formulas with added carbohydrate. Cereal was offered earlier than usual with equal frequency in both types of feeding. There were fewer infants having firm to hard stools among those receiving a formula without added carbohydrate than among infants taking a formula with added carbohydrate.

The incidence of "colic" may be somewhat less in that group of infants receiving formula without added carbohydrate.

It would seem that formulas prepared with water and fresh whole cow's milk or evaporated cow's milk without additional carbohydrate are quite satisfactory for infant feeding.

FACTORS AFFECTING RETENTION OF NITROGEN AND CALCIUM IN PERIOD OF GROWTH

IX. Corticotropin (ACTH)

J. A. JOHNSTON, M.D.
AND
M. J. SWEENEY, M.D.
DETROIT

AN INCREASE in the excretion of nitrogen following the administration of corticotropin (ACTH) is reported in animals and in humans. The explanation offered by Albright [1] is that it represents loss of protoplasm and may be attributed to the secretion of the "sugar" hormone from the adrenal cortex. It is considered an antianabolic rather than a catabolic effect. Clark's [2] work with tagged glycine supports the concept of antianabolism. That diversion by way of gluconeogenesis is not adequate to explain quantitatively the phenomenon as brought out by Ingle,[3] who feels that inhibition of the oxidation of glucose may be an added factor to explain the loss. Much of the effect may be further conditioned by the state of the organism, the diversion of protein being diminished or prevented by previous administration of dextrose and accentuated by insulin (Engel).[4] In animals the effect is not sustained, an adaptation occurring in the rat in about 10 days, permitting a return to a positive nitrogen balance.

Using the low calcium intake and studying patients with panhypopituitarism, Bartter and co-workers [5] reported a rise in the urinary calcium in nine of 10 courses of corticotropin administration, with a fall after treatment was stopped. They point out that in Cushing's syndrome osteoporosis is a prominent feature. Levin and co-workers [6] also reported an increase in both stool and urine calcium in a balance study on an adult with periarteritis nodosa, and with intake constant the tendency was for the balance to become negative.

From the Department of Pediatrics, Henry Ford Hospital, and the Edsel B. Ford Institute for Medical Research.

1. Albright, F.: Cushing's Syndrome: Its Pathological Physiology, Its Relationship to the Adreno-Genital Syndrome, and Its Connection with the Problem of the Reaction of the Body to Injurious Agents ("Alarm Reaction" of Selye), Harvey Lect. (1942-1943) **38**:123, 1943.

2. Clark, I.: Effect of Cortisone on Protein Metabolism in the Rat as Studied with Isotopic Glycine, Federation Proc. **9**:161 (March) 1950.

3. Ingle, D. J.: The Biologic Properties of Cortisone: A Review, J. Clin. Endocrinol. **10**:1312 (Oct.) 1950.

4. Engel, F. L.: Studies on the Nature of the Protein Catabolic Response to Adrenal Cortical Extract: Accentuation by Insulin Hypoglycemia, Endocrinology **45**:170 (Aug.) 1949.

5. Bartter, F. C.; Fourman, P.; Albright, F.; Forbes, A. P.; Jefferies, W. M.; Griswold, G.; Dempsey, E.; Bryant, D., and Carroll, E.: The Effect of Adrenocorticotropic Hormone in Panhypopituitarism, J. Clin. Invest. **29**:950 (July) 1950.

6. Levin, M. H.; Adams, W. S.; Beck, W. S.; Goldman, R., and Bassett, S. H.: Prolonged Treatment of a Case of Periarteritis Nodosa with ACTH: The Effective Dose as Measured by Metabolic Balances, J. Clin. Endocrinol. **11**:375 (April) 1951.

Hill and associates,[7] in the study of corticotropin and thyroid function, concluded that the adrenal steroids appeared to have a calorigenic action and at the same time to suppress thyroid activity through pituitary inhibition and that their effect on the basal metabolic rate would be a resultant of these two opposing actions.

Balance studies for nitrogen and calcium are presented on children receiving corticotropin for rheumatic fever, rheumatoid arthritis, and lupus erythematosus. When the clinical condition permitted, determinations of basal metabolism were made at sporadic intervals. An analyzed diet proportioned calorically 15% protein, 35% fat, and 50% carbohydrate was offered and refusals analyzed, but intake was based on appetite. This usually increased markedly after the administration of corticotropin, and the caloric intake was correspondingly raised, the proportions being kept constant. Our findings may not be directly comparable with those reported above for the following reasons: (1) we are dealing with children in the growth period; (2) we were permitting an increase in intake as dictated by appetite, which consistently increased with the hormone; (3) the subjects were presumably normal endocrinologically, and (4) all had a disease process, and these were in varying states of activity. In that sense, the studies here reported are measures of pharmacological rather than a physiological effect of the hormone. In addition, it can be assumed that the adrenal response to corticotropin will be conditioned by the capacity of the cortex to produce steroids, which in turn will vary with age and sex. Some such mechanism must be invoked to explain the differences reported here in calcium metabolism. The effect on the basal metabolic rate can also be expected to be different in a child whose active disease process is abruptly suppressed by the hormone and in the chronic rheumatoid whose initial metabolism is not elevated.

METHODS

The methods used were given in detail in the first two papers[8] of this series. The corticotropin used was either Wilson's or Armour's, though in one observation National's was used. Adequacy of response was checked with the eosinophile count. In the charts nitrogen metabolism is plotted in three-day periods. For calcium the urine is recorded in three-day periods, but the stool is averaged for longer periods, since no significance can be assigned to three-day fecal excretions on full intakes.

REPORT OF CASES

Case 1 (balance study Aug. 3 to Nov. 12, 1950).—Mary L., 13 years old, born May 7, 1937, was admitted July 16, 1950, complaining of painless swelling of feet and legs of about seven days' duration and moderate shortness of breath of three to four days' duration. She had been completely well until about six weeks prior to admission, when circinate skin lesions developed beginning on the hands and spreading to the trunk and other extremities. The lesions itched and were sometimes painful.

Physical examination revealed a slightly elevated temperature, pitting edema of lower legs and feet, slight periorbital edema, and a circinate, red, scaly, maculopapular rash over the trunk and extremities. The blood pressure was recorded as 138/70. The laboratory data were essentially normal except for an erythrocyte sedimentation rate of 30 and a 1+ reaction for albumin.

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7. Hill, S. R.; Reiss, R. S.; Forsham, P. H., and Thorn, G. W.: Effect of ACTH and Cortisone on Thyroid Function, J. Clin. Endocrinol. **10**:1375 (Nov.) 1950.

8. Johnston, J. A., and Maroney, J. W.: Factors Affecting Retention of Nitrogen and Calcium in Period of Growth: Effect of Thyroid on Nitrogen Retention, Am. J. Dis. Child. **58**:965 (Nov.) 1939; Factors Affecting Retention of Nitrogen and Calcium in Period of Growth: Effect of Thyroid on Calcium Retention, ibid. **58**:1186 (Dec.) 1939.

TABLE 1.—*Balance Observation in Case 1*

3-Day Period No.	Dates, 1950	Nitrogen, Gm./Day				Calcium, Gm./Day				B. M. R.*		R. Q.	Basal Cal.	Wt., Lb.	Ht., In.	Diet Cal.	E. S. R.	Comment
		Average Urine	Average Stool	Intake	Balance	Average Urine	Average Stool	Intake	Balance	B.	W.							
1	8/ 3- 8/ 5	12.94	0.73	12.16	—1.51	0.149	1.263	1.444	+0.032	....	....	....	.....	....	....	1,900	..	1st corticotropin course (49 days) begun 7/18
2	8/ 6- 8/ 8	9.14	0.00	12.16	+3.02	0.128	0.000	1.444	+1.316	....	....	....	.....	....	....	.....	18	.....
3	8/ 9- 8/11	7.68	0.79	15.08	+6.56	0.129	1.213	1.744	+0.402	....	....	....	.....	....	....	2,400	..	.....
4	8/12- 8/14	8.54	1.00	15.03	+5.49	0.085	1.443	1.744	+0.216	....	....	....	.....	....	....	.....	..	Dose 12 mg. every 6 hr.
5	8/15- 8/17	12.01	3.15	15.79	+0.63	0.192	2.320	1.922	+0.590	....	....	....	.....	....	....	2,600	27	.....
6	8/18- 8/20	10.00	1.01	16.12	+5.11	0.123	1.275	2.002	+0.604	....	....	....	.....	....	....	.....	..	.....
7	8/21- 8/23	10.53	0.66	16.64	+5.45	0.137	0.787	1.924	+1.000	....	....	....	.....	....	....	.....	..	.....
Average		10.11	1.05	14.70	+3.54	0.135	1.186	1.892	+0.671	....	....	....	.....	....	....	.....	..	.....
8	8/24- 8/26	14.47	1.27	16.64	+0.90	0.129	0.987	1.924	+0.808	....	....	....	.....	....	....	.....	..	Gradual withdrawal of drug begun
9	8/27- 8/29	11.60	1.33	16.38	+3.45	0.130	2.273	2.314	—0.098	....	....	....	.....	....	....	.....	..	.....
10	8/30- 9/ 1	11.43	1.17	16.38	+3.78	0.220	1.458	2.314	+0.636	....	....	....	.....	....	....	2,600	..	.....
11	9/ 2- 9/ 4	13.80	1.28	17.68	+2.51	0.188	1.505	1.898	+0.205	—7	±0	0.88	1,202	81½	59¼	.....	..	Complete withdrawal 9/4
Average		12.85	1.01	16.77	+2.91	0.169	1.556	2.112	+0.387	....	....	....	.....	....	....	.....	..	.....
12	9/ 5- 9/ 7	9.77	1.26	17.68	+6.65	0.175	1.249	1.868	+0.474	....	....	....	.....	....	....	.....	..	.....
13	9/ 8- 9/10	10.04	1.25	17.42	+6.13	0.154	1.235	1.867	+0.458	±0	+6	0.79	1,310	84½	59¼	2,600	..	.....
14	9/11- 9/13	8.61	1.21	16.52	+6.70	0.206	1.274	1.997	+0.517	—4	+2	0.87	1,272	86½	59¼	.....	..	.....
15	9/14- 9/16	10.14	1.46	16.78	+5.18	0.236	1.463	1.883	+0.194	+5	+11	0.77	1,387	88½	59¼	.....	..	.....
16	9/17- 9/19	9.39	1.21	15.48	+4.88	0.234	0.948	1.959	+0.777	....	....	....	.....	....	....	.....	22	.....
17	9/20- 9/22	7.73	1.25	14.18	+5.20	0.219	1.244	1.725	+0.267	....	....	....	1,430	90½	59½	.....	45	.....
18	9/23- 9/25	8.87	1.00	15.17	+5.21	0.258	1.119	1.725	+0.348	+6	+13	0.79	.....	....	....	2,600	..	.....
19	9/26- 9/28	9.35	1.53	15.54	+4.66	0.284	1.399	2.198	+0.515	....	....	....	.....	....	....	.....	..	.....
Average		9.24	1.28	16.09	+5.57	0.221	1.244	1.905	+0.440	....	....	....	.....	....	....	.....	..	.....
20	9/29-10/ 1	16.13	0.84	15.54	—1.43	0.162	0.982	2.198	+1.104	+10	+8	0.78	1,497	95¼	60	.....	..	2d course of corticotropin begun, 60 mg. daily
21	10/ 2-10/ 4	16.24	0.95	15.28	—1.91	0.200	1.294	1.992	+0.498	....	....	....	.....	....	....	.....	20	.....
22	10/ 5-10/ 7	13.58	1.40	16.12	+1.14	0.158	0.697	1.480	+0.575	—11	—4	0.85	1,231	97	60	.....	22	.....
23	10/ 8-10/10	17.72	1.13	14.56	—4.29	0.239	1.320	1.742	+0.183	....	....	....	.....	....	....	.....	15	Dose 90 mg. daily; bed rest
Average		15.92	1.08	15.37	—1.63	0.189	1.061	1.840	+0.590	....	....	....	.....	....	....	.....	..	.....
24	10/11-10/13	13.01	0.95	14.56	+0.60	0.212	1.005	1.742	+0.525	....	....	....	.....	....	....	.....	..	Dose 12 mg. every 6 hr.; gradual withdrawal begun
25	10/14-10/16	11.31	1.87	17.16	+3.98	0.206	1.742	1.846	+0.102	—13	—10	0.84	1,231	97	60	.....	..	.....
26	10/17-10/19	9.41	2.45	14.42	+2.56	0.238	1.512	1.807	+0.057	....	....	....	.....	....	....	.....	29	.....
27	10/20-10/22	6.66	2.55	14.94	+5.73	0.165	1.168	1.937	+0.604	±0	±0	0.79	1,394	98¼	60	.....	..	.....
28	10/23-10/25	7.89	1.44	14.94	+5.61	0.245	1.121	1.937	+0.571	....	....	....	.....	....	....	.....	28	Moderate activity
29	10/26-10/28	6.08	1.46	11.25	+3.71	0.144	1.358	1.709	+0.267	—13	—4	0.71	1,242	100½	60	.....	25	Moderate activity
Average		9.06	1.79	14.54	+3.69	0.202	1.317	1.839	+0.320	....	....	....	.....	....	....	.....	..	.....
30	10/29-10/31	9.56	0.88	11.25	+0.81	0.262	0.880	1.709	+0.627	....	....	....	.....	....	....	.....	..	Complete withdrawal; moderate activity continued to end of study
31	11/ 1-11/ 3	8.35	1.19	13.72	+4.18	0.237	1.771	1.763	—0.245	+6	+15	0.77	1,502	101⅝	60	.....	..	.....
32	11/ 4-11/ 6	7.55	1.84	13.72	+4.33	0.226	1.533	1.763	+0.204	....	....	....	.....	....	....	.....	28	.....
33	11/ 7-11/ 9	6.80	1.34	11.32	+3.18	0.150	0.930	1.491	+0.402	+4	+12	0.78	1,468	101⅝	60	.....	..	.....
34	11/10-11/12	6.53	1.23	11.32	+3.53	0.142	0.692	1.491	+0.657	....	....	....	.....	....	....	.....	..	.....
Average		7.76	1.30	12.26	+3.30	0.208	1.123	1.655	+0.229	....	....	....	.....	....	....	.....	..	.....

* In this and succeeding tables, B. indicates the basal metabolic rate referred to in the Boothby-Sandiford table and W. to the prediction made with the Wetzel grid.

Two days after admission a full-blown picture of acute disseminated lupus erythematosus developed, with the butterfly rash over the face, evidence of acute nephritis, and pancarditis. She appeared to be critically ill. Administration of corticotropin was started, with dramatic clinical improvement during the next three days. She received corticotropin for about 50 days, and clinically, except for erythema multiforme, the disease seemed to be in a state of complete

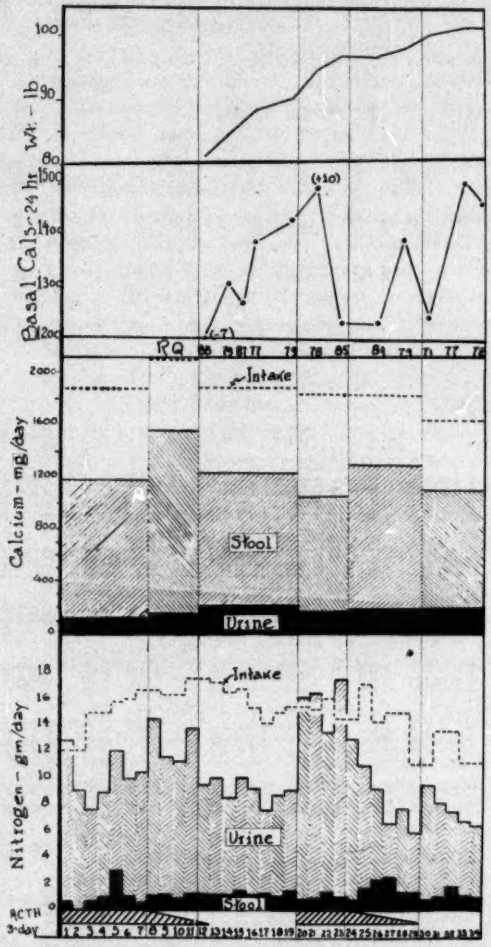

Chart 1 (Case 1).—Balances for a 13-year-old girl with lupus erythematosus: Observations start on the 17th day of a 49-day course of corticotropin. Nitrogen balance is negative for the first three days; then excretion falls and intake rises, the balance becoming strongly positive. A second course produces a negative balance for 12 days; a positive balance follows the decrease in dose. For calcium no control was available for the first course. During the second course urinary and fecal excretions are less than in the periods preceding and following, with resulting increased retention. A significant fall in basal metabolism results from corticotropin. A steady rise of 300 Cal. correlates with reactivation of disease. The fall with the second course is most likely the result of suppression of the disease process.

remission. However, 18 days after corticotropin therapy was discontinued she began to show evidence of carditis, and another 30-day course of corticotropin was given.

Since that time she had had several exacerbations and remissions of symptoms. She was treated with cortisone and corticotropin. However, in spite of extensive therapy, she had a gradual downhill course and died on April 14, 1951, of uremia secondary to renal failure.

Nitrogen and calcium balance studies were obtained during (1) the last 33 days of the first 49-day course of corticotropin, (2) a 24-day period without therapy, (3) a second course of 30 days of corticotropin, and (4) a 15-day after-period.

The nitrogen balance was negative in the first three-day period of the observation, which represented the 17th to the 19th day of administration of corticotropin. It then became strongly positive because of a fall in urine nitrogen and rise in intake; administration of the hormone was continued for an additional 21 days, 12 mg. every six hours, and then the amount was slowly decreased during the next 12 days to complete withdrawal. Retentions doubled in the after-period. A negative balance followed in the second course, the balance becoming positive when the dose was reduced from 90 to 48 mg. and then gradually withdrawn.

The lowest urinary calcium value is noted in the first corticotropin period, following which there is a gradual rise in all remaining periods independent of the administration of the hormone. This could be understood as a result of prolonging bed rest, though moderate activity was allowed from the 28th three-day period on. Balances are positive for calcium throughout. There is a suggestive correlation between stool and basal metabolism, large losses coinciding with depressed metabolism rates. These determinations were not possible in the first half of the study, when the child was acutely ill.

Basal metabolism determinations could not be made until the 11th period. There is a significant variation in basal calories, a steady rise of 300 Cal. occurring after the withdrawal of corticotropin. This probably reflects reactivation of the disease process, a sharp fall occurring on the resumption of the hormone administration. There is the contributing factor of the accumulation of large amounts of nitrogen, something which has previously been shown[9] to be accompanied with a rise in basal calories.

Case 2 (balance study Aug. 3 to Sept. 19, 1950).—Verna K., born May 24, 1933, had her first attack of rheumatic fever in 1938; she was treated with bed rest for five months. A recurrence in 1946 was treated with two months of bed rest. A third attack in 1949, with heart failure, was also treated with bed rest, for three months. One week before her admission on July 22, 1950, there was a fourth recurrence, with heart failure also. The heart showed evidence of mitral stenosis with insufficiency, and there was fibrillation. She responded well to treatment with salicylates, digitalis, and oxygen, although when corticotropin was introduced, the erythrocyte sedimentation rate was elevated.

The doses of corticotropin used were the following: Wilson's, 12 mg. daily from Aug. 11 to 13, 20 mg. daily from Aug. 14 to 19, and 20 mg. daily from Aug. 26 to Sept. 3; Armour's, 15 mg. on Sept. 4, 10 mg. daily from Sept. 5 to 7, and 5 mg. on Sept. 8. In addition to the corticotropin, she received digitoxin, 0.2 mg. a day, and ammonium chloride, 3 gm. daily for three days, alternating with three days without ammonium chloride.

There were clinical improvement and a fall in the erythrocyte sedimentation rate from 40 to 21. Three weeks after the conclusion of the second course, it had risen again to 47.

Concerning the nitrogen balance data, appetite was extremely poor, and the intake of this item was only 5 gm. until corticotropin administration was started. This was followed by a striking increase in intake and positive balances in spite of high urinary nitrogen values. Calcium balance in the short foreperiod of six days and in the first corticotropin period of 10 days was negative; from then on balances became positive, both with and without corticotropin, because of a very marked increase in intake. Changes correlate better with intake than anything else, and it is not clear that corticotropin had any specific effect other than to stimulate increased intake. Relatively high urinary calcium could be expected to result from ammonium chloride, but values are no higher during corticotropin therapy than in the final after-period.

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9. Johnston, J. A., and Maroney, J. W.: Relationship of Basal Metabolism to Dietary Intake, Am. J. Dis. Child. **51**:1039 (May) 1936.

TABLE 2.—*Balance Observation in Case 2*

3-Day Period No.	Dates, 1950	Nitrogen, Gm./Day				Calcium, Gm./Day				B. M. R.		Basal Cal.	Wt., Lb.	Ht., In.	Diet Cal.	E. S. R.	Comment
		Average Urine	Average Stool	Intake	Balance	Average Urine	Average Stool	Intake	Balance	B.	W.						
1	8/ 3- 8/ 5	3.08	1.32	4.89	+0.49	0.156	0.306	0.576	+0.114	+19	+18	1,478	85½	65¼	1,800	40	.....
2	8/ 6- 8/ 8	4.37	0.65	4.89	−0.13	0.088	1.536	0.576	−1.048	....	....	.....	....	....	.....	..	.....
Average		3.72	0.98	4.89	+0.19	0.122	0.921	0.576	−0.467	....	....	.....	....	....	.....	..	.....
3	8/ 9- 8/11	7.22	0.55	12.88	+5.11	0.140	0.927	1.204	+0.137	....	....	.....	....	....	2,000	..	1st course corticotropin begun 8/10
4	8/12- 8/14	6.83	1.09	12.88	+4.96	0.164	1.445	1.204	−0.405	+4	+4	1,317	80¼	64½	.....	..	.....
5	8/15- 8/17	8.12	3.67	11.88	+0.09	0.175	1.627	1.184	−0.618	....	....	.....	....	....	.....	21	.....
6	8/18- 8/20	10.91	1.38	13.23	+0.94	0.156	2.377	1.643	−0.890	−7	+10	1,140	80¾	64½	2,200	20	Withdrawal 8/19
Average		8.27	1.67	12.72	+2.78	0.158	1.594	1.308	−0.444	....	....	.....	....	....	.....	..	.....
7	8/21- 8/23	9.45	0.73	14.08	+3.90	0.211	1.186	1.628	+0.281	....	....	.....	....	....	.....	43	.....
8	8/24- 8/26	9.44	1.05	14.08	+3.59	0.171	1.328	1.628	+0.129	....	....	.....	....	....	.....	..	2d course begun 8/26
Average		9.44	0.89	14.08	+3.75	0.191	1.232	1.628	+0.205	....	....	.....	....	....	.....	..	.....
9	8/27- 8/29	11.44	2.05	15.75	+2.26	0.209	2.796	2.225	−0.780	−12	−4	1,090	86½	64½	.....	..	.....
10	8/30- 9/ 1	10.89	1.10	15.75	+3.76	0.197	1.203	2.225	+0.825	....	....	.....	....	....	2,500	..	.....
11	9/ 2- 9/ 4	11.44	1.66	17.00	+3.90	0.237	2.220	1.825	− 632	−6	−7	1,178	88½	64½	.....	..	.....
12	9/ 5- 9/ 7	13.87	0.17	17.00	+2.96	0.269	0.333	1.825	+1.223	....	....	.....	....	....	.....	..	.....
13	9/ 8- 9/10	12.79	0.92	16.75	+3.04	0.182	1.485	1.900	+0.233	....	....	.....	....	....	.....	22	.....
Average		12.09	1.18	16.45	+3.18	0.219	1.607	2.000	+0.174	....	....	.....	....	....	.....	..	.....
14	9/11- 9/13	13.74	1.31	16.00	+0.95	0.295	1.987	2.025	−0.257	....	....	.....	....	....	.....	..	Withdrawal 9/11
15	9/14- 9/16	13.64*	0.84	16.25	+1.77	0.262*	0.989	1.925	+0.674	+12	+12	1,437	92½	....	.....	..	.....
16	9/17- 9/19	13.55	2.17	16.25	+0.53	0.229	1.872	1.925	−0.176	....	....	.....	....	....	.....	..	.....
Average		13.64	1.44	16.16	+1.08	0.262	1.616	1.958	+0.080	....	....	.....	....	...	.....	..	E. S. R. was 47 on 10/7

* Urine specimen lost; figure is average of preceding and following specimen.

Basal metabolism is elevated in the foreperiod and falls significantly with corticotropin therapy, rising again after withdrawal. The elevation is presumably a function of active infection, the fall a result of the suppression of the disease process. The rise on the withdrawal was accompanied with a rise in the erythrocyte sedimentation rate.

CASE 3 (balance study April 1 to Aug. 4, 1950).—Hugh P., born Jan. 16, 1935, at 5 years had a history of frequent tonsillitis, which led to tonsillectomy and adenoidectomy, without apparent benefit. At 10 years he had acute polyarthritis and responded well to therapy with

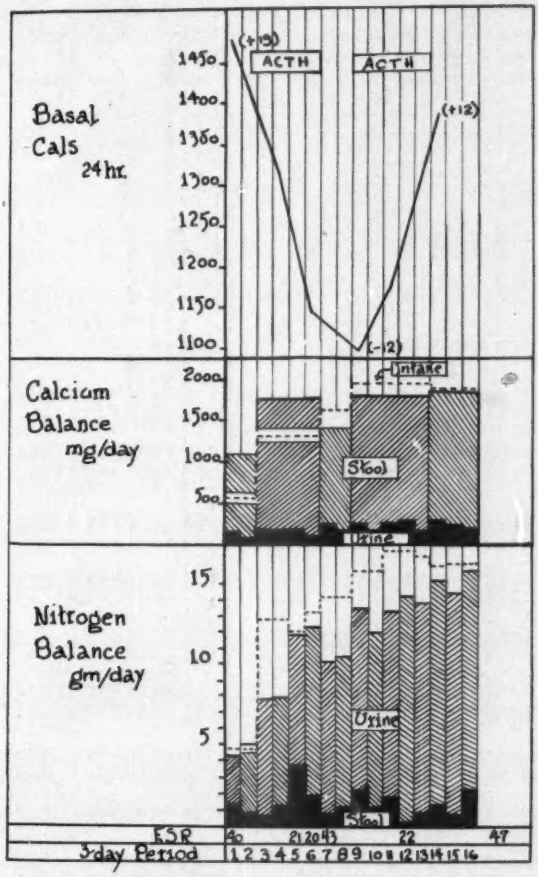

Chart 2 (Case 2).—Balances for an 18-year-old girl with acute rheumatic carditis: A significant fall in basal metabolism occurs with corticotropin administration; there is a prompt rebound when this is stopped, probably reflecting reactivation of the disease, as judged by a rise in the erythrocyte sedimentation rate. Intake of nitrogen and calcium increase markedly. Urine nitrogen rises, but with the increased intake only one short negative balance is obtained. Negative calcium balances are noted during the first course, positive during the second.

salicylates. Several months later there was recurrence of polyarthritis, with pancarditis. There was gradual improvement with rest and salicylate therapy. At 13 years there was recurrence of the joint symptoms and carditis, with failure requiring oxygen, meralluride injection (mercuhydrin sodium solution®), and rest.

TABLE 3.—*Balance Observation in Case 3*

3-Day Period No.	Dates, 1950	Nitrogen, Gm./Day				Calcium, Gm./Day				Basal Cal.	B. M. R.		Wt., Lb.	Ht., In.	Diet Cal.	Comment
		Average Urine	Average Stool	Intake	Balance	Average Urine	Average Stool	Intake	Balance		B.	W.				
1	4/ 1- 4/ 3	12.02	0.81	12.21	−0.62	0.428	1.803	1.256	−0.475	.....	....	....	.....	....	2,400	.....
2	4/ 4- 4/ 6	10.09	0.29	12.21	+1.83	0.529	0.380	1.256	+0.347	.....	....	....	.....	....	.....	.....
3	4/ 7- 4/ 9	8.63	1.11	10.65	+0.91	0.349	1.143	1.239	−0.253	.....	....	....	.....	....	.....	.....
4	4/10- 4/12	9.08	1.00	9.42	−0.66	0.363	1.467	1.126	−0.704	.....	....	....	.....	....	.....	.....
5	4/13- 4/15	8.79	0.77	10.05	+0.49	0.288	0.904	1.152	−0.040	1,512	−8	+6	97¾	66½	.....	.....
6	4/16- 4/18	10.19	0.43	11.32	+0.70	0.328	0.373	1.205	+0.504	.....	....	....	.....	....	.....	.....
Average		9.80	0.73	10.98	+0.45	0.381	0.928	1.205	−0.104	.....	....	....	.....	....	.....	.....
7	4/19- 4/21	7.47	1.09	6.09	−2.47	0.280	1.773	0.749	−1.304	1,476	−10	−2	.....	.....	.....	Temperature elevation 4/21-4/23
8	4/22- 4/24	7.94	0.86	9.64	+0.84	0.273	0.934	1.308	+0.101	.....	....	....	.....	....	.....	Vitamin C 4/24-5/11
9	4/25- 4/27	5.92	0.43	10.00	+3.65	0.222	0.753	1.270	+0.295	1,492	−9	−5	96½	....	.....	.....
10	4/28- 4/30	6.52	0.59	9.97	+2.86	0.266	0.996	1.251	−0.011	.....	....	....	.....	....	.....	.....
11	5/ 1- 5/ 3	6.85	1.02	12.13	+4.26	0.223	1.562	1.398	−0.387	1,444	−11	±0	97½	....	.....	.....
12	5/ 4- 5/ 6	7.80	0.92	12.13	+3.41	0.303	1.379	1.398	−0.284	.....	....	....	.....	....	.....	.....
Average		7.06	0.82	9.90	+2.09	0.261	1.233	1.229	−0.205	.....	....	....	.....	....	.....	.....
13	5/ 7- 5/ 9	.....	0.79	10.48	+2.48	0.413	1.389	1.353	−0.449	.....	....	....	.....	....	.....	.....
14	5/10- 5/12	8.75	0.62	10.48	+1.11	0.331	0.870	1.353	+0.152	1,380	−15	−3	97½	65¾	.....	.....
15	5/13- 5/15	10.70	0.53	12.04	+0.82	0.319	0.849	1.299	+0.131	.....	....	....	.....	....	.....	.....
16	5/16- 5/18	7.57	0.00	12.04	+4.48	0.216	0.000	1.299	+1.083	.....	....	....	.....	....	.....	.....
17	5/19- 5/21	9.25	1.07	11.18	+3.86	0.188	1.576	1.318	−0.446	1,528	−6	+6	98	....	.....	.....
18	5/22- 5/24	9.19	0.97	11.18	+1.02	0.307	1.492	1.318	−0.481	.....	....	....	.....	....	.....	.....
Average		8.28	0.66	11.23	+2.29	0.296	1.029	1.323	−0.002	.....	....	....	.....	....	.....	.....
19	5/25- 5/27	9.52	0.98	11.99	+1.49	0.308	1.231	1.272	−0.267	1,509	−9	+4	100	66½	.....	.....
20	5/28- 5/30	6.92	1.01	12.02	+4.09	0.217	1.374	1.243	−0.348	.....	....	....	.....	....	.....	.....
21	5/31- 6/ 2	7.69	0.69	11.52	+3.14	0.192	1.217	1.193	−0.216	1,536	−6	+6	99½	....	.....	.....
22	6/ 3- 6/ 5	8.62	0.82	7.92	−1.52	0.184	1.307	1.085	−0.406	.....	....	....	.....	....	.....	.....
23	6/ 6- 6/ 8	4.95	0.89	8.55	+2.71	0.184	0.849	0.951	−0.082	1,418	−13	−1	96½	....	.....	.....
24	6/ 9- 6/11	5.86	0.52	13.02	+6.64	0.186	0.444	1.628	+0.998	.....	....	....	.....	....	.....	.....
Average		7.26	0.82	10.84	+2.76	0.212	1.070	1.229	−0.053	.....	....	....	.....	....	.....	.....
25	6/12- 6/14	9.35	1.12	13.22	+2.75	0.248	1.600	1.614	−0.234	.....	....	....	.....	....	2,400	Bicycle exercise begun 6/12
26	6/15- 6/17	10.61	0.00	12.50	+1.89	0.479	0.000	1.614	+1.135	1,514	−9	+4	100	66½	.....	.....
27	6/18- 6/20	6.73	1.07	7.65	−0.15	0.223	1.512	0.816	−0.919	.....	....	....	.....	....	.....	.....
28	6/21- 6/23	6.94	1.06	12.36	+4.36	0.169	0.523	1.292	+0.600	1,408	−13	−1	98½	....	.....	.....
29	6/24- 6/26	9.52	0.54	12.36	+2.30	0.232	0.433	1.292	+0.627	.....	....	....	.....	....	.....	.....
30	6/27- 6/29	9.96	0.93	13.67	+2.78	0.262	1.591	1.693	−0.160	1,548	−5	+6	99½	....	.....	.....
Average		8.85	0.79	11.96	+2.32	0.269	0.943	1.387	+0.175	.....	....	....	.....	....	.....	.....
31	6/30- 7/ 2	10.03	0.73	13.67	+2.91	0.176	1.035	1.693	+0.482	.....	....	....	.....	....	.....	Corticotropin begun 6/30, 5 mg every 6 hr.
32	7/ 3- 7/ 5	10.79	0.93	14.22	+2.50	0.154	1.440	1.720	+0.126	1,442	−13	−1	103	.....	.....	.....
33	7/ 6- 7/ 8	11.51	0.61	14.22	+2.10	0.137	1.122	1.720	+0.461	.....	....	....	.....	....	.....	.....
34	7/ 9- 7/11	12.84	0.74	15.42	+1.84	0.121	1.330	1.936	+0.485	1,459	−12	−1	104	....	.....	.....
35	7/12- 7/14	11.26	0.27	16.66	+5.13	0.122	0.464	2.004	+1.418	.....	....	....	.....	....	.....	.....
36	7/15- 7/17	12.58	0.87	17.86	+4.41	0.148	1.591	2.052	+0.313	.....	....	....	.....	....	.....	.....
Average		11.50	0.69	15.34	+3.15	0.144	1.163	1.854	+0.547	1,450	−12	−1	.....	....	.....	Corticotropin withdrawn
37	7/18- 7/20	11.56	0.89	17.86	+5.41	0.105	1.699	2.052	+0.248	1,339	−19	−9	104½	66½	2,400	.....
38	7/21- 7/23	12.25	1.00	15.66	+2.41	0.134	1.967	1.929	−0.172	.....	....	....	.....	....	.....	.....
39	7/24- 7/26	11.47	0.85	15.66	+3.34	0.127	1.393	1.929	+0.409	.....	....	....	.....	....	.....	.....
40	7/27- 7/29	7.13	0.67	14.46	+6.66	0.091	0.957	1.785	+0.737	1,502	−10	+2	.....	....	.....	.....
41	7/30- 8/ 1	10.70	1.12	15.38	+3.56	0.181	1.667	1.760	−0.088	.....	....	....	.....	....	.....	.....
42	8/ 2- 8/ 4	10.20	1.02	13.46	+2.24	0.167	1.331	1.640	+0.142	1,452	−13	−1	.....	....	.....	.....
Average		10.55	0.93	15.41	+3.93	0.134	1.502	1.849	+0.213	.....	....	....	.....	....	.....	.....

The present studies were undertaken when he had been at best rest about five months. Compensation was good, but he was receiving digitoxin, salicylates 40 grains (2.59 gm.) a day, ferric sulfate 5 grains (0.32 gm.) a day, and one capsule of a multivitamin preparation (multicebrin®) a day. The corticotropin used was Wilson's, of which he received 5 mg. every six hours. On July 24 he received penicillin preparatory to a dental extraction.

The observation occupied 126 days, divided into seven periods of 18 days. The variables introduced were large doses of ascorbic acid, exercise, and corticotropin. Administration of 600 mg. daily of ascorbic acid, given while he was still at bed rest, correlates with a significant rise in nitrogen storage, the urinary output falling 2.7 gm. a day. The calcium balance, however, already negative, became more so. A definite fall in the urine calcium was more than offset by a fecal loss. Gentle exercises, consisting in pushing a mounted wheel for a minute twice a day, increasing by one minute, were immediately followed by a shift from negative to positive calcium

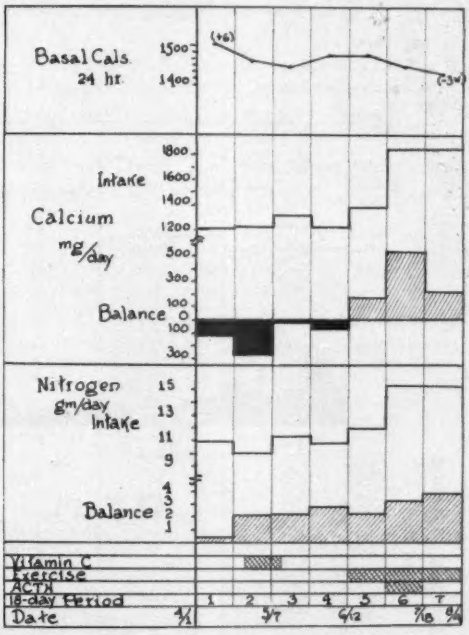

Chart 3 (Case 3).—A summary of the entire observation on a 15-year-old boy with rheumatic fever: This summary is made to bring out the point that before the observation period during which corticotropin was given, a negative balance for calcium, presumably resulting from bed rest, became positive with activity. A large dose of ascorbic acid was accompanied with a significant increase in nitrogen retention. The mechanism is not clear. Periods 5, 6, and 7 of this chart are presented in detail in Chart 4.

balance in the fifth 18-day period. Much of this is referable to an increase in intake, but there was also a fall in stool calcium. Urinary output rose. Corticotropin was given throughout the sixth 18-day period, 5 mg. every six hours. From June 30 to July 13 the sedimentation rate fell; on June 13 it was 28, and on July 13 it was 7. The eosinophile count was 302 on June 30 and 74 on July 5. The immediate effect of corticotropin was a marked increase in the intake of both nitrogen and calcium. Urinary nitrogen rose from 8.85 to 11.50 gm. a day, but this loss was more than offset by the increased intake, so that the balance rose from 2.32 to 3.15 gm. a day. Urinary calcium fell from 269 to 144 mg. a day. This together with the increased intake resulted in the balance going from 175 to 547 mg. a day. It is probably significant that this effect is in contrast with that obtained when another subject (Earl H.) was completely at bed rest.

CASE 4 (balance study June 7 to July 20, 1950).—Earl H., born Aug. 4, 1937, had acute rheumatic fever with carditis at the time of study. In March, 1950, this 12½-year-old boy had a throat infection which was followed in 10 days by fatigue, anorexia, abdominal pain, and generalized aching of the legs. The next day his ankles became swollen, hot, and tender, and the knees, elbows, and hands became similarly involved. This condition lasted eight weeks, during which time secondary anemia developed and rheumatic nodules appeared.

On examination he showed evidence of carditis and pericarditis. His temperature was 102 F., his pulse rate 132, his respiratory rate 32. Electrocardiography showed a P-R interval of

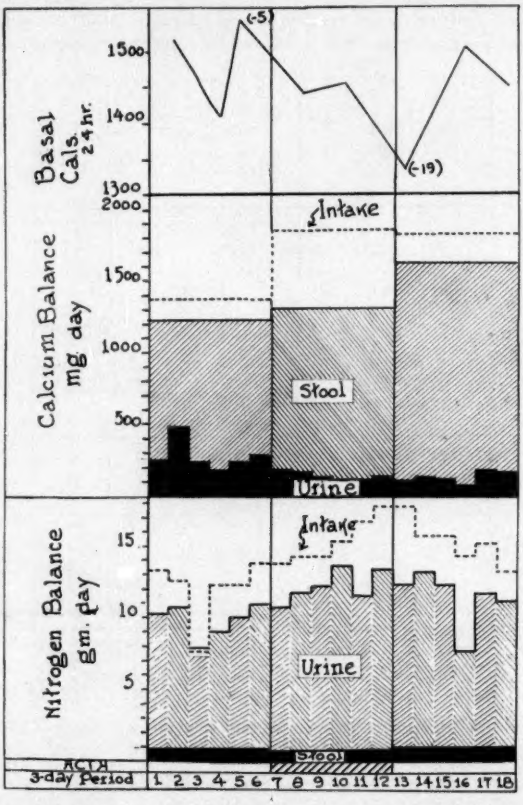

Chart 4 (Case 3).—Periods 5, 6, and 7 (each 18 days) of Chart 3 presented in detail: Nitrogen excretion rises but is offset by increased intake, resulting in an increased retention. A small increase in stool calcium, a diminished output of urine calcium, and a marked increase in intake result in an increased balance. Basal calories show no significant change until the hormone is withdrawn, when there is a significant but transient fall. This patient's disease process was inactive during the study, except for a slight elevation of erythrocyte sedimentation rate to 28.

0.18 second, an R-R interval of 0.48 second, and a Q-T interval of 0.26 second. He was considered to have acute rheumatic pancarditis with mitral insufficiency and aortic insufficiency with moderate prolongation of circulation time. He was too ill for us to obtain a control balance period before treatment was started. Treatment was begun with 40 mg. of Armour's corticotropin (June 9 to June 15) and continued with 80 mg. (June 15 to June 30); a fall in

eosinophile count occurred on June 16. With a shift to 40 mg. of Wilson preparation on July 1, the count remained low (18). Administration of corticotropin was gradually decreased in amount, and dosage was stopped on July 9, after 31 days of therapy. Treatment other than with corticotropin included administration of potassium chloride, 1 gm. three times a day, penicillin, meralluride injection, and, on June 13, 100 mg. of vitamin C. Clinical response was excellent. No recurrence has been noted in an eight-month follow-up.

To comment on balance data, negative nitrogen balances became positive on the withdrawal of the hormone, because of a fall in urinary output while the intake was increasing. Calcium balances were negative throughout on intakes that would normally be expected to produce positive storage, but several variables were present: (1) inactivity was absolute, (2) no vitamin D was given, and (3) meralluride injection and potassium chloride were used. The urinary output was as great in the after-period as during the treatment. Fecal output was larger in the after-period than during the treatment, but so was the intake.

TABLE 4.—*Balance Observation in Case 4*

		Nitrogen, Gm./Day				Calcium, Gm./Day					
3-Day Period No.	Dates, 1950	Average Urine	Average Stool	Intake	Balance	Average Urine	Average Stool	Intake	Balance	Diet Cal.	Comment
1	6/ 7- 6/ 9	8.47	0.91	9.88	+0.50	0.284	0.902	1.110	−0.076	1,900	1st course corticotropin (Armour) begun 6/9, 40 mg. daily
2	6/10- 6/12	5.96	1.56	10.30	+2.78	0.128	0.826	1.186	+0.232	.....	.....
3	6/13- 6/15	11.51	1.13	12.80	+0.16	0.213	1.280	1.427	−0.066	.....	Armour's, 80 mg. daily
Average		8.65	1.20	10.99	+1.14	0.208	1.003	1.241	+0.023	.....	.....
4	6/16- 6/18	11.41	1.90	12.49	−0.82	0.183	1.976	1.429	−0.730	.....	.....
5	6/19- 6/21	12.88	1.77	12.49	−2.16	0.184	1.701	1.429	−0.456	.....	.....
6	6/22- 6/24	14.33	1.27	13.35	−2.25	0.133	1.582	1.551	−0.164	2,000	.....
7	6/25- 6/27	16.62	0.42	15.74	−1.30	0.229	0.430	1.815	+1.156	2,400	.....
8	6/28- 6/30	15.00	1.85	15.55	−1.30	0.242	1.627	1.743	−0.126	.....	Armour's, 80 mg. daily
Average		14.05	1.44	13.92	−1.57	0.194	1.463	1.593	−0.064	.....	.....
9	7/ 1- 7/ 3	14.33	1.51	15.60	−0.24	0.304	1.633	1.752	−0.185	.....	Wilson's, 20 mg. daily
10	7/ 4- 7/ 6	12.97	1.57	15.60	+1.06	0.233	2.224	1.800	−0.185	.....	Wilson's, 15 mg. daily
11	7/ 7- 7/ 9	13.43	2.69	15.60	−0.52	0.217	2.454	1.800	−0.871	.....	Corticotropin withdrawn
Average		13.58	1.96	15.60	−0.02	0.251	2.103	1.784	−0.570	.....	.....
12	7/10- 7/12	9.83	1.82	17.80	+6.15	0.171	1.124	2.016	+0.721	.....	.....
13	7/13- 7/15	11.79	1.50	17.80	+4.51	0.297	1.560	2.016	+0.249	.....	.....
14	7/16- 7/18	10.53	2.80	17.64	+4.51	0.233	3.900	1.975	−2.158	.....	.....
15	7/19- 7/20	9.54	1.40	16.56	+5.62	0.352	1.374	1.582	−0.144	.....	.....
Average		10.37	1.88	17.45	+5.20	0.241	1.989	1.897	−0.350	.....	.....

CASE 5 (balance study Jan. 18 to Feb. 25, 1951).—Marlene P., born Nov. 3, 1937, had rheumatoid arthritis at the time of study. She was a 13-year-old girl with a history of pain and swelling of joints and fever of two years' duration. The initial episode followed an acute upper respiratory tract infection. Examination showed fusiform swelling of the phalangeal joints and contracture deformity of the little finger. An eczematous skin lesion was over the elbows. There was general glandular enlargement. The heart was of normal size. There was a systolic murmur over the precordium. The electrocardiogram showed a P-R interval of 0.12 second, a QRS interval of 0.05 second. Glucose tolerance was normal; fat absorption was impaired, as judged by the single-dose vitamin A absorption curve giving a five-hour reading of 47.

In addition to the corticotropin (40 mg. daily of the Wilson preparation), she was receiving 5 grains of acetylsalicylic acid about five times a day for pain. She was ambulatory during the study.

Regarding the balance study, intake was constant, and during the control period of 15 days she stored normal amounts of calcium and nitrogen. The administration of corticotropin was followed by (1) marked increase in urinary nitrogen, producing a negative balance; (2) a threefold increase in the output of urinary calcium, diminishing the positive balance but not

rendering it negative (the after-period of six days is not long enough for significance to be attached to the fecal loss, though the urinary drop is significant), and (3) gain in weight, followed by loss on withdrawal of corticotropin. The basal metabolism falls from a peak figure of 1,305 Cal. per 24 hours in the period preceding the administration of corticotropin to a low of 1,044 Cal. per 24 hours (basal metabolic rate of +6 to —14 in the Boothby-Sandiford table) in the period following its discontinuance, with a recovery to 1,190 Cal. six days later. No significant change is evident during the administration; the fall noted on withdrawal is seen in other chronic cases in which the disease process has not caused an initial elevation.

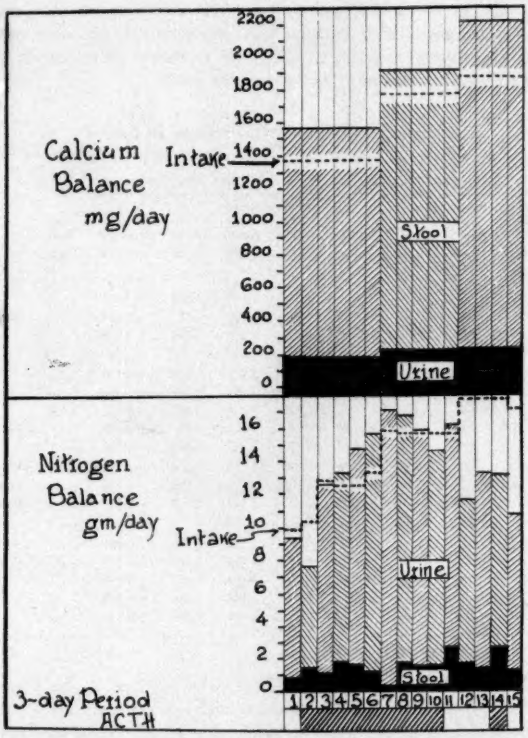

Chart 5 (Case 4).—Balances for a 12½-year-old boy with acute rheumatic fever with carditis: The negative nitrogen balance becomes positive on withdrawal of corticotropin. Calcium balance is negative throughout, contrary to expectancy; however, several variables were present: inactivity was absolute, no vitamin D was given, and meralluride injection and potassium chloride were used.

Case 6 (balance study Aug. 11 to Oct. 3, 1950).—William G., born July 18, 1940, a 10-year-old boy having rheumatoid arthritis, dated his illness to the age of 2 years, at which time a respiratory infection developed and was followed by a migratory type of arthritis. The diagnosis of acute rheumatic fever was made, and he was observed at bed rest for three months, during which time swelling and stiffness of the ankles and wrists were noted. Periodic exacerbations have occurred, with fever, pain, and swelling of wrists, knees, and ankles; treatment was with salicylates and physical therapy. Each episode left him with greater impairment, the range of motion in joints decreasing and contractures developing.

TABLE 5.—*Balance Observation in Case 5: Diet 2,200 Calories*

3-Day Period No.	Dates, 1951	Nitrogen, Gm./Day				Calcium, Gm./Day				B. M. R.		R. Q.	Total Cal.	Wt., Lb.	Ht., In.	Comment
		Average Urine	Average Stool	Intake	Balance	Average Urine	Average Stool	Intake	Balance	B.	W.					
1	1/18- 1/20	10.80	1.25	14.78	+2.73	0.093	0.973	1.628	+0.562	+5	+10	0.80	1,296	76	67¾	.....
2	1/21- 1/23	10.87	1.19	14.78	+2.72	0.083	1.100	1.628	+0.445	....	....	....	.....	....	....	.....
3	1/24- 1/26	11.62	1.57	14.56	+1.37	0.101	1.506	1.628	+0.021	−2	+3	0.76	1,202	74¾	68¼	.....
4	1/27- 1/29	9.58	1.21	13.56	+2.77	0.091	1.013	1.668	+0.564	....	....	....	.....	....	....	.....
5	1/30- 2/ 1	9.71	1.16	14.44	+3.57	0.110	1.116	1.492	+0.266	+6	+12	0.78	1,305	75¾	68¼	.....
Average		10.51	1.27	14.42	+2.63	0.096	1.141	1.609	+0.372	+3	+8	0.78	1,268	75¾	68¼	.....
6	2/ 2- 2/ 4	10.10	1.39	14.44	+2.95	0.089	1.241	1.492	+0.162	....	....	....	.....	....	....	Corticotropin (Wilson) begun 2/2, 40 mg. daily
7	2/ 5- 2/ 7	10.93	1.24	11.75	−0.42	0.088	1.117	1.394	+0.189	−1	+4	0.76	1,248	78¼	68¼	.....
8	2/ 8- 2/10	12.00	0.98	11.75	−1.23	0.109	0.747	1.394	+0.538	....	....	....	.....	....	....	.....
9	2/11- 2/13	13.17	1.20	14.17	−0.20	0.195	1.271	1.504	+0.038	−3	+2	0.84	1,233	80	68	.....
10	2/14- 2/16	14.59	1.01	15.71	+0.11	0.217	1.257	1.734	+0.260	....	....	....	.....	....	....	.....
11	2/17- 2/19	16.32	1.17	13.73	−3.76	0.364	1.382	1.404	−0.342	....	....	....	.....	....	....	Corticotropin withdrawn 2/19
Average		12.85	1.16	13.57	−0.42	0.177	1.169	1.487	+0.141	....	....	....	.....	....	....	.....
12	2/20- 2/22	13.65	1.21	13.73	−1.13	0.116	1.499	1.404	−0.211	−14	−10	0.86	1,044	73¾	68	.....
13	2/23- 2/25	11.05	1.83	15.05	+2.17	0.134	1.545	1.624	−0.055	....	....	....	.....	....	....	.....
Average		12.35	1.52	14.39	+0.52	0.125	1.522	1.514	−0.133	....	....	....	.....	....	....	.....

Aside from joint deformities, results of examination were essentially negative, and the electrocardiogram was normal. Sedimentation rate was 36, hemoglobin 13.2 gm., white blood cells 8,800, with 61% polymorphonuclear leucocytes, 2% eosinophiles, 36% lymphocytes, and 1% monocytes. Nonprotein nitrogen was 33 mg. per 100 cc. Fat absorption was impaired, as judged by the vitamin A tolerance test (41 mg. per 100 cc.). Oral glucose tolerance test showed normal results. The basal metabolic rate was —15 according to the Boothby-Sandiford tables and —9 according to the Wetzel grid.

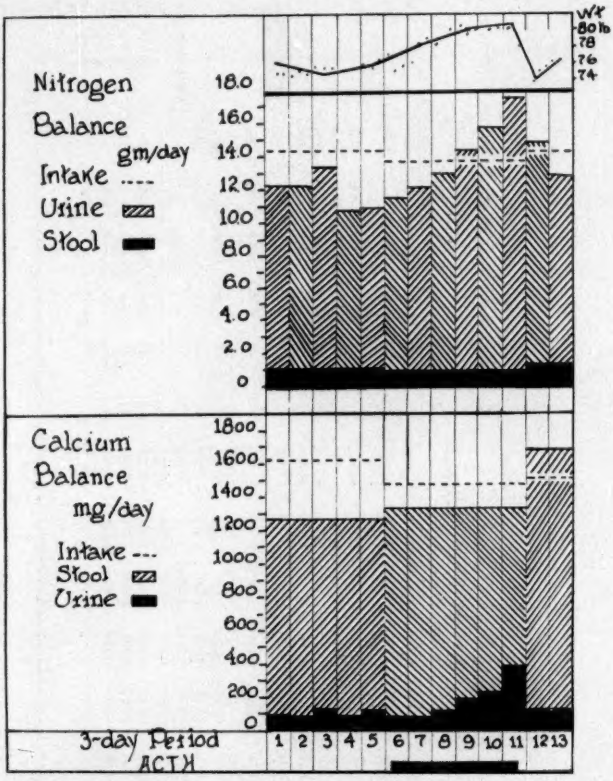

Chart 6 (Case 5).—Balances for a 13-year-old girl with rheumatoid arthritis: Corticotropin produces increased urinary nitrogen and a negative balance with intake constant. There is a very significant rise in urinary calcium, a slight rise in fecal output, and a diminished retention. Basal calories (not charted) are unaffected until withdrawal of corticotropin, when there is a significant fall.

He received 32 mg. daily of Wilson's corticotropin from Aug. 23 through Sept. 14. During this time he received a few minutes of bed bicycle exercise daily to offset the tendency toward the negative balances incidental to bed rest.

The clinical response was excellent; he walked with assistance for the first time in eight months.

To comment on the balance study, the nitrogen balance became negative because of an increased urinary output of nearly 2 gm. a day, too large to be offset by an increased intake of 0.6 gm. a day. A marked rebound followed the withdrawal of the hormone, the urine nitrogen falling from 11.54 to 6.64 gm. a day.

TABLE 6.—*Balance Observation in Case 6: Diet 2,000 Calories*

3-Day Period No.	Dates, 1950	Nitrogen, Gm./Day				Calcium, Gm./Day				B. M. R.		Basal Cal.	Wt., Lb.	Ht., In.	Comment
		Average Urine	Average Stool	Intake	Balance	Average Urine	Average Stool	Intake	Balance	B.	W.				
1	8/11- 8/13	12.12	0.77	12.29	—0.60	0.146	1.060	1.345	+0.139	....	....	.....	....	....	.....
2	8/14- 8/16	7.37	0.86	11.29	+3.06	0.086	0.819	1.325	+0.420	—15	—9	1,250	95	54½	.....
3	8/17- 8/19	9.95	0.39	11.29	+0.95	0.093	0.501	1.325	+0.731	....	....	.....	....	....	.....
4	8/20- 8/22	9.42	0.06	11.55	+1.47	0.123	0.797	1.342	+0.422	—13	—6	1,296	96¼	55½	.....
Average		9.71	0.67	11.60	+1.22	0.112	0.794	1.334	+0.428	....	....	.....	....	....	Corticotropin (Wilson), 32 mg. daily, begun 8/23
5	8/23- 8/25	9.58	0.84	11.75	+1.33	0.108	1.143	1.322	+0.076	....	....	.....	....	....	.....
6	8/26- 8/28	8.66	0.51	11.55	+2.38	0.123	0.685	1.622	+0.814	—17	—10	1,243	97½	....	.....
7	8/29- 8/31	13.20	0.71	11.60	—2.31	0.134	0.805	1.721	+0.782	....	....	.....	....	....	Exercise, bed bicycle, begun 8/29
8	9/ 1- 9/ 3	11.56	0.76	12.09	+0.28	0.147	1.125	1.401	+0.129	....	....	.....	....	....	.....
9	9/ 4- 9/ 6	12.35	0.95	12.60	—0.70	0.084	1.379	1.401	—0.062	....	....	.....	....	....	.....
10	9/ 7- 9/ 9	14.76	0.81	13.05	—2.52	0.090	0.802	1.388	+0.386	....	....	.....	....	....	.....
11	9/10- 9/12	12.00	0.71	12.25	—0.46	0.105	0.835	1.523	+0.583	—21	—17	1,149	96¼	....	.....
12	9/13- 9/15	10.22	1.17	12.45	+1.06	0.131	1.520	1.443	—0.203	....	....	.....	....	....	Corticotropin withdrawn 9/14
Average		11.54	0.81	12.23	—0.12	0.114	1.048	1.476	+0.314	....	....	.....	....	....	.....
13	9/16- 9/18	6.99	0.64	11.14	+3.51	0.100	0.634	1.365	+0.631	—11	—7	1,284	....	....	.....
14	9/19- 9/21	6.85	0.87	10.14	+2.42	0.102	1.346	1.185	—0.263	....	....	.....	....	....	.....
15	9/22- 9/24	6.46	0.53	9.96	+2.97	0.069	1.005	1.035	—0.009	—12	—9	1,257	97½	....	.....
16	9/25- 9/27	7.00	0.59	10.56	+2.97	0.083	1.800	1.425	—0.458	....	....	.....	....	....	.....
17	9/28- 9/30	4.78	0.49	7.52	+2.25	0.044	0.455	0.991	+0.492	....	....	.....	....	....	.....
18	10/ 1-10/ 3	7.76	0.43	11.51	+3.32	0.090	0.558	0.843	+0.195	....	....	.....	....	....	.....
Average		6.64	0.59	10.14	+2.91	0.081	0.966	1.145	+0.099	....	....	.....	....	....	.....

There is a rise in intake of calcium of 142 mg. and a rise in calcium in the stools of 254 mg., with no significant change in the urine output, resulting in a decreased retention of 114 mg. a day. The fall in urine calcium in the two after-periods may be referable to both an increase in activity and a reduction in intake.

The basal metabolic rate falls significantly from a high of 1,296 Cal. per 24 hours to a low of 1,149 Cal. per 24 hours, with a recovery after withdrawal.

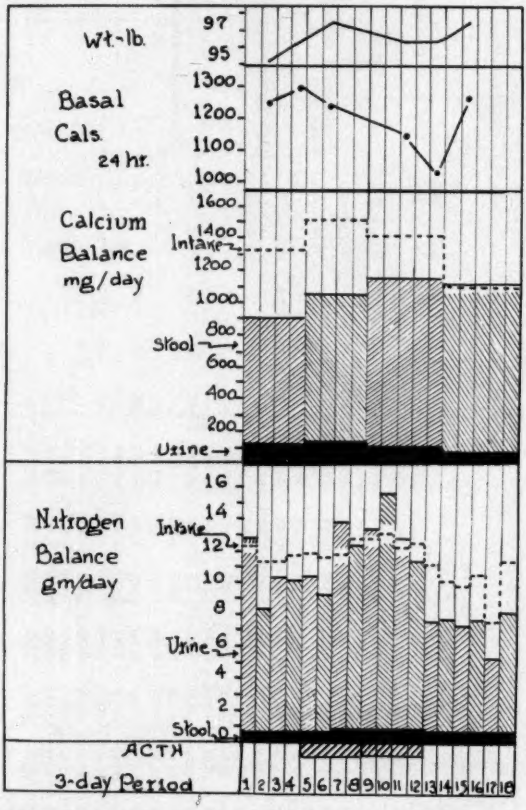

Chart 7 (Case 6).—Balances for a 10-year-old boy with rheumatoid arthritis and elevated erythrocyte sedimentation rate: Corticotropin produced increased nitrogen loss not compensated by increased intake. There is increased fecal calcium with diminished retention. Basal calories fall significantly, but there is a recovery after the withdrawal of the hormone.

COMMENT

In using a preparation such as corticotropin, whose effect depends upon the release of steroids from the adrenal cortex, it should be expected that the response would be conditioned by age and sex, by the state of the metabolic pool, and by the disease condition which is being treated. Very different responses were elicited in a 15-year-old boy with inactive rheumatic fever and a 13-year-old girl with rheumatoid arthritis. Interpretation would be less confusing on fixed intakes,

but with the illnesses being treated, an adequate intake often could not be taken in the control period, and the striking effect on appetite could not be ignored as an effect to be studied and welcomed therapeutically.

The effect on nitrogen metabolism when corticotropin was given to children with rheumatic fever, rheumatoid arthritis, and lupus erythematosus was a marked increase in the urinary output and an equally striking increase in intake resulting from improved appetite. This increase in intake was often sufficient to prevent the development of a negative balance. A sharp fall in output followed either a reduction in dose or withdrawal of the hormone. When the hormone was administered over a long period, a tendency toward adaptation was noted, the initial high urinary losses falling. In one case (Hugh P.) a positive balance became even more so with corticotropin administration, the increased intake more than offsetting the increase in urinary output.

The effect of calcium metabolism was not consistent. In dealing with unrestricted intake, data are felt to lack significance for periods of less than 15 days [10] because of stool lag. In four studies of significant length, fecal calcium rose in two, fell in one, and was unchanged in one; urine calcium rose in two and fell in two; intake rose in two, fell in one, and was unchanged in one; the balance rose in two, fell in one, and was unchanged in one. Inactivity causing a depressed utilization may have been a stronger factor influencing calcium metabolism. When exercise had resulted in a negative balance becoming positive in one case, a further increase in retention followed corticotropin therapy, resulting from both a fall in urine loss and a rise in intake. It could be expected that any marked fall in basal metabolism would be accompanied with increased fecal losses, and this was noted in Case 2.

The effect on basal metabolism varied with the clinical condition being treated. When the hormone suppressed an active disease process (lupus erythematosus and acute rheumatic fever), a significant fall from the initially elevated rate occurred, the rate rising promptly again if reactivation occurred on withdrawal of the hormone. In the chronic and the inactive case no significant change occurred during the administration of the hormone, but a marked fall followed the withdrawal, presumably the result of pituitary depression.

SUMMARY

Balance studies for nitrogen and calcium, with intermittent determinations of basal metabolism, are reported for children with lupus erythematosus, rheumatic fever, and rheumatoid arthritis receiving corticotropin. The effects varied with the condition when treatment was started. In all cases urine nitrogen rises, but increases in intake tend to offset this. Calcium changes vary with activity, with basal metabolism, and with intake. Basal metabolism falls if an active disease process is being suppressed. A transient depression on the basal rate follows withdrawal if infection does not reactivate.

Part of the expense of this study was defrayed by a grant from the Michigan Heart Association. Dr. O. H. Gaebler, of the Edsel B. Ford Research Institute, supervised the metabolic determinations. Mr. Gustav Stolz gave technical assistance. Dr. V. G. Behrmann supervised the determinations of basal metabolism.

10. Porter-Levin, T.: Calcium and Phosphorus Metabolism of Normal Pre-School Children: Successive Balance Studies Showing the Range of Variation in Calcium and Phosphorus Storage, J. Am. Dietet. A. **9**:22 (May) 1933.

RELATION BETWEEN SOCIOECONOMIC STATUS AND BODY SIZE IN BOYS SEVEN TO TEN YEARS OF AGE

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IT IS THE purpose of this paper to assemble and discuss the results from several studies relating to differences in average body size among children representing various socioeconomic levels. Specifically, consideration is restricted to investigative work carried out in the United States and Canada, to the age period from 7 to 10 years, and to materials on one sex (boys). Within this age-sex-geographic scaffold, the objectives of the paper include colligating the available research literature, reporting new findings from a 1950 investigation, and epitomizing the present status of knowledge on the problem.

The problem can be expressed in the following more generalized form: What is the relation between socioeconomic status and body size in North American children of elementary-school age? This amount of latitude in formulation is justifiable, since (*a*) the ages 7 to 10 typify the elementary-school years and (*b*) the findings reported on girls are similar to those on boys.

A few prefatory comments are in order concerning what socioeconomic status comprises and how estimates of it are obtained. Socioeconomic status is neither a precisely defined concept[1] nor a variable that is described from study to study by means of a single standardized scale. Different investigators have seen fit to estimate it through information on family income,[2] father's occupation,[3] resources of the home,[4] type of neighborhood,[5] and receipt of services on a nonpay basis in contrast with a fee basis.[6] Despite this diversity of approach, it has been found that practically all such items lead to growth relationships that are compatible.

There is common agreement that socioeconomic status should be conceived as a variable which can be reduced to a series of categories (e. g., occupational categories such as unskilled and semiskilled; commercial, skilled and minor managerial;

From the School of Health and Physical Education, University of Oregon.

1. Meredith, H. V.: Physical Growth from Birth to Two Years: 1. Stature, Studies in Child Welfare, Iowa City, University of Iowa, 1943, Vol. 19.

2. Wise, F. C., and Meredith, H. V.: The Physical Growth of Alabama White Girls Attending WPA Preschools, Child Develop. **13**:165-174 (Sept.) 1942.

3. Porter, W. T.: The Growth of St. Louis Children, Tr. Acad. Sc., St. Louis **6**:263-380, 1894.

4. Stiles, C. W., and Wheeler, G. A.: Heights and Weights of Children, Pub. Health Rep. **30**:2990-3003, 1915.

5. Hedger, C.: The School Children of the Stockyards District, Tr. 15th Internat. Cong. Hygiene and Demography **3**:170-188, 1913.

6. Bakwin, H., and Bakwin, R. M.: Body Build in Infants: V. Anthropometry in the New-Born, Human Biol. **6**:612-626 (Dec.) 1934.

professional and major managerial), each representing a different combination of a group of subvariables. From the standpoint of physical growth, the subvariables known or thought to be differential include health care, diet, personal hygiene, sanitation, and selective mating. Certainly the constellations of these factors differ for children of the indigent class and those of the wealthy class, for children representing the vocationally semiskilled and those representing the professional vocations.

Among the available studies of body size on North American boys 7 to 10 years of age, there are three in which the socioeconomic continuum was divided into two parts. For all three information on "occupation of the principal wage earner of the family" constituted the raw material subjected to bipartite classification.

The earliest of these investigations was made between 1875 and 1880 in Boston, Mass.,[7] the second between 1895 and 1900 in Washington, D. C.,[8] and the most recent between 1935 and 1940 in 16 states scattered from Alabama to Minnesota and California to Virginia.[9] The reports increase in anthropometric scope with order of publication: Bowditch studied height and weight on white boys partly of American-born parentage and partly of Irish-born parentage; MacDonald studied height, weight, sitting height, and head girth on white boys of American-born parentage, and O'Brien and co-workers studied a still larger number of measurements on "the general run of white American-born boys."

Bowditch and MacDonald used the occupational categories: (1) "professional or mercantile," and (2) "skilled or unskilled." In the study by O'Brien and co-workers the split was made at a different point, placing skilled workers in the first category and assigning to the second only the "semiskilled or unskilled." Table 1 presents—at each annual age from 7 to 10 years—the obtained differences between comparable pairs of body-size means from these bipartite schemes. It also gives the size of the sample used in obtaining each mean.

Selected generalizations are the following:

1. Average over-all size of the body is larger for United States schoolboys representing the upper occupational groups than for those representing the lower occupational groups.

2. The mean of the 12 height differences is 1.3 cm. (½ in.). The 12 weight differences give a mean of 0.6 kg. (1¼ lb.).

3. For the other measurements, the differences are smallest in head girth, intermediate in arm girth, and largest in chest girth.

4. A trend of increasing difference with age is indicated, i. e., the upper occupational groups exceed the lower occupational groups by somewhat larger amounts at 10 years than at 7 years.

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7. Bowditch, H. P.: The Growth of Children: A Supplementary Investigation, Boston, Rand, Avery & Co., 1879, reprinted from Rep. Bd. Health Mass. **10**:35-62, 1879.

8. MacDonald, A.: Experimental Study of Children, Including Anthropological and Psycho-Physical Measurements of Washington School Children, Reports of the Commissioner of Education, United States Bureau of Education, Washington, D. C., Government Printing Office, Vol. 1, Pt. 1.

9. O'Brien, R.; Girshick, M. A., and Hunt, E. P.: Body Measurements of American Boys and Girls for Garment and Pattern Construction, United States Department of Agriculture, Miscellaneous Publication No. 366, 1941.

In discussing their results, both Bowditch and O'Brien and co-workers recognized that although body-size differences were found between children divided into two socioeconomic levels, the basis of classification used need not necessarily have been the sole cause. They called attention to the possibility that part of the obtained differences may have resulted from insufficient control of the racial factor, e. g., from "predominance" of North European anthropologic types in the upper socioeconomic category or from "larger admixture" of South European anthropologic types in the lower.

The series of investigations to be considered next constitute a logical extension of those just summarized. Again, there are three in the series, and all employ

TABLE 1.—*Body Size and Socioeconomic Status of North American Boys Seven to Ten Years of Age: Differences Between Means from Bipartite Classification of Boys in Terms of Occupation of "Principal Wage Earner of Family"*

Investigation	Difference, Mean of U Minus Mean of L *							
	7 Yr.	8 Yr.	9 Yr.	10 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.
	Height, Cm.				Weight, Kg.			
Bowditch (1879) †	1.5	1.6	1.2	1.2	0.3	0.5	0.6	0.6
MacDonald (1899) †	0.5	0.6	1.0	1.9	0.0	—0.1	0.4	0.4
O'Brien and co-workers (1941) ‡	1.5	1.4	1.6	1.8	0.8	0.9	1.1	1.4
	Sitting Height, Cm.				Head Girth, Cm.			
MacDonald (1899) †	0.3	0.3	0.6	0.8	0.3	0.1	0.3	0.3
	Chest Girth, Cm.				Waist Girth, Cm.			
O'Brien and co-workers (1941) ‡	0.6	0.7	0.8	1.0	0.3	0.4	0.5	0.6
	Upper-Limb Length, Cm.				Hip Width, Cm.			
O'Brien and co-workers (1941) ‡	0.6	0.7	0.7	0.7	0.3	0.3	0.4	0.4
	Arm Girth, Cm.				Leg Girth, Cm.			
O'Brien and co-workers (1941) ‡	0.3	0.4	0.5	0.6	0.4	0.5	0.5	0.6

	Number of Subjects *							
	7 Yr.		8 Yr.		9 Yr.		10 Yr.	
	U	L	U	L	U	L	U	L
Bowditch (1879)	174	728	189	778	187	757	180	715
MacDonald (1899)	201	196	277	327	310	330	351	346
O'Brien and co-workers (1941)	2,268	2,277	2,603	2,781	2,872	3,057	3,116	3,177

* The upper part of the vocation scale is symbolized by U, the lower part by L.
† L data are from children of skilled, semiskilled, and unskilled workers, U data from children of all other types of workers.
‡ L data are from children of semiskilled and unskilled workers, U data from children of all other types of workers.

vocational data to estimate socioeconomic status. Two impose special controls with reference to the racial variable, while all three resort to tripartite sectioning of the vocational distribution and thereby secure two widely separated (terminal) segments for comparison.

The previously utilized study by Bowditch includes means for height of boys representing the "professional" and the "unskilled" groups. That is, in addition to his twofold occupational analyses, Bowditch reports height findings from threefold analysis. In effect, the occupational distribution was divided into three parts; the middle part was excluded, and the two tail parts were subjected to separate and comparative study. Quantitatively, the "unskilled" tail encompassed approximately 42% of the distribution, the excluded portion about 55%, and the "professional" segment 3%. The amounts by which the height means for the "professional" group surpassed those for the "unskilled" group are shown in Table 2.

Dearborn and co-workers [10] made accessible data for several measures of body size taken over the years 1923 to 1927 on boys 7 to 10 years of age attending the public schools in Medford, Beverly, and Revere, Mass. Each boy was placed in an occupational category and also assigned a racial classification. The racial classifications were made by the phenotypic method of the physical anthropologist, i. e., they were based upon combinations of "items such as skin pigmentation, facial features, eye and hair color, and form of hair."

It was possible for me [11] to extract from these materials of Dearborn and co-workers data on two series of boys representing the same racial class but

TABLE 2.—*Body Size and Socioeconomic Status of North American Boys Seven to Ten Years of Age: Differences Between Means from Terminal Segments of the Occupational Distribution*

Investigation	Difference, Mean of UT Minus Mean of LT *							
	7 Yr.	8 Yr.	9 Yr.	10 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.
	Height, Cm.				Weight, Kg.			
Bowditch (1879) †	2.6	2.1	2.8	2.6	...	...	...	...
Meredith (1941) ‡	1.4	1.9	2.1	2.2	1.0	1.3	1.5	1.9
Meredith (1950) ‡	2.2	...	...	2.9	1.2	...	...	2.0
	Sitting Height, Cm.				Head Width, Cm.			
Meredith (1941)	0.4	0.6	0.6	0.7	0.2	0.1	0.2	0.2
Meredith (1950)	0.8	...	...	1.2	...	...	...	...
	Chest Girth, Cm.				Abdomen Girth, Cm.			
Meredith (1950)	0.8	...	...	1.2	0.9	...	...	1.3
	Shoulder Width, Cm.				Hip Width, Cm.			
Meredith (1950)	0.5	...	...	0.7	0.3	...	...	0.3
	Upper-Limb Length, Cm.				Lower-Limb Length, Cm.			
Meredith (1950)	1.1	...	...	1.5	1.4	...	...	1.7
	Arm Girth, Cm.				Leg Girth, Cm.			
Meredith (1950)	0.3	...	...	0.7	0.4	...	...	0.7

Investigation	Number of Subjects *							
	7 Yr.		8 Yr.		9 Yr.		10 Yr.	
	UT	LT	UT	LT	UT	LT	UT	LT
Bowditch (1879)	27	391	30	408	26	394	27	380
Meredith (1941) §	38	93	46	110	55	122	55	124
Meredith (1950)	55	51	...	...	...	...	43	40

* The professional and managerial tail is symbolized by UT, the semiskilled and unskilled tail by LT.
† UT indicates "professional"; LT, "unskilled."
‡ UT indicates "professional and managerial"; LT, "semiskilled and unskilled."
§ The numbers given are for height, weight, and sitting height, the numbers for head width are approximately one-half of these.

markedly different socioeconomic levels. The racial class was that designated "North European"; the socioeconomic levels were "professional or important managerial" and "semiskilled or unskilled." Percentages of the total occupational distribution in these terminal segments approximated 14 and 33 respectively (leaving 53% in the excluded "small business, commercial, and skilled-trade" category). Table 2 shows the differences obtained between means at each age for height, weight, sitting height, and head width.

10. Dearborn, W. F.; Rothney, J. W. M., and Shuttleworth, F. K.: Data on the Growth of Public School Children, Washington, Society for Research in Child Development, National Research Council, 1938, Vol. 3, No. 1, Serial No. 14.

11. Meredith, H. V.: Unpublished study, 1941.

During 1950 I collected data covering 11 aspects of body size on boys 7 and 10 years of age enrolled in the 17 elementary schools of Public School District No. 4, Eugene, Ore.[12] The anthropometric examinations were supplemented with parent interviews in which information was obtained on the ethnic background of the family and the vocation of the principal wage earner. These items made it possible to compare terminal segments of the vocational distribution, using only data from boys whose ancestors came from northwest Europe. The total number of boys of northwest European ancestry was 212 at age 7 years and 159 at age 10 years. Of these, approximately 26% fell in the "professional and managerial" category, about 49% in the excluded (middle) category, and 25% in the "semiskilled and unskilled" category. Table 2 gives the differences between each pair of means for the complete series of 11 measurements.

Findings from this table and from comparison with Table 1 are the following:

1. In every one of the measures of body size studied United States schoolboys representing the professional and managerial classes are larger than those representing the semiskilled and unskilled classes.

2. For height the mean of the 10 "terminal segment" differences in Table 2 is 2.4 cm. (practically 1 in.). The mean of the six adjacent weight differences is 1.5 kg. (3¼ lb.). Terminal-segment differences larger than 0.5 cm. are found for sitting height, upper-limb length, lower-limb length, chest girth, abdomen girth, and shoulder width.

3. On the whole, the bipartite differences in Table 1 are appreciably smaller than the terminal-segment differences in Table 2, i. e., there is a direct relation between magnitude of dissimilarity in body size and amount of separation between the occupational categories compared.

Those who have utilized information on "occupation of the principal wage earner in the family" have recognized that this does not yield a completely valid measure of socioeconomic status. Bowditch, in his 1879 study, pointed out that "persons described as following the same occupation may often have very different social positions."[13] O'Brien and co-workers, 1941, noted that "living conditions of families" are indicated only "roughly" by occupations of the principal wage earners.[14]

An alternate estimate of socioeconomic status was used by Robertson,[15] Weisman,[16] and Hopkins.[17] Each of these investigators compared the body size of boys attending public elementary schools in the best and poorest sections of a North American city.

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12. Research supported by a grant from the Graduate School, University of Oregon. Full cooperation was given by Superintendent Clarence Hines, Dr. Madeline Marr, and also the principals, teachers, nurses, custodians, parents, and pupils.

13. Bowditch, [7] p. 35.

14. O'Brien, Girshick, and Hunt,[9] p. 114.

15. Robertson, T. B.: Studies on the Growth of Man: The Variability of the Weight and Stature of School Children and Its Relationship to Their Physical Welfare, Am. J. Physiol. **41**:547-554 (Nov.) 1916.

16. Weisman, S. A.: Contour of the Chest in Children: Environment, Am. J. Dis. Child. **49**:52-59 (Jan.) 1935.

17. Hopkins, J. W.: Height and Weight of Ottawa Elementary School Children of Two Socio-Economic Strata, Human Biol. **19**:68-82 (May) 1947.

The subjects for Robertson's study were two groups of boys between 8 and 9 years of age obtained in Oakland, Calif. The sampling procedure consisted in selecting "at random" (*a*) 50 boys from among those attending "a school situated in a relatively wealthy residential section of the city" and (*b*) 50 boys from among those attending "a school which was situated in a relatively poor industrial district, inhabited mainly by factory operatives." Means were computed from height and weight data on each group.

Weisman's study was made in Minneapolis at "four representative schools in the best section and four in the poorest section." It affords height and weight medians at each annual age from 7 to 10 years.

TABLE 3.—*Body Size and Socioeconomic Status of North American Boys Seven to Ten Years of Age: Differences Between Means for Boys Attending Schools in the "Best" (B) and "Worst" (W) Section of Oakland, Calif., Minneapolis, and Ottawa, Ont., Canada*

Investigation	Difference, Mean of B Minus Mean of W				
	7 Yr.	8 Yr.	8½ Yr.	9 Yr.	10 Yr.
			Height, Cm.		
Robertson (1916)	...	...	6.3	...	...
Weisman (1935)	2.3	2.3	...	2.0	3.7
Hopkins (1947)	2.5	2.6	...	2.9	3.0
			Weight, Kg.		
Robertson (1916)	...	...	2.8	...	...
Weisman (1935)	0.7	0.8	...	1.0	1.9
Hopkins (1947)	1.1	1.3	...	1.7	1.8
			Number of Subjects		
Robertson (1916)					
"Wealthy district"	...	...	50	...	...
"Factory district"	...	...	50	...	...
Weisman (1935)					
"Best section"	146	145	...	148	180
"Poorest section"	84	119	...	144	128
Hopkins (1947)					
"Better-class area"	235*	235*	...	235*	235*
"Less prosperous area"	190*	190*	...	190*	190*

* Approximate number.

The records analyzed by Hopkins were amassed during the years 1933 to 1945 at six public elementary schools in Ottawa, Ont., Canada. Three of the schools drew from "predominantly better-class residential districts" and three from "less prosperous areas of the city." Hopkins claimed no more than "aggregate" socioeconomic differentiation ("There was of course considerable intra-school variation"), and he drew attention to the fact that his poorer-class schools included many sons of "artisans, tradespeople and government employees of the clerical grades."

Table 3 displays the differences between the central-tendency values obtained by each investigator (more precisely, what are displayed are the differences between medians for height and weight from Weisman and between means for height and weight from Robertson and Hopkins). The following are seen:

1. The differences reported by Robertson are much larger than those obtained by Weisman or Hopkins. It appears probable that Robertson's results register the operation of differential ethnic as well as socioeconomic variables: the parents of his sample of schoolboys from the Oakland factory district "included a large proportion of individuals of foreign birth."

2. The composite means for the series of differences from Weisman and Hopkins are 2.9 cm. (slightly over 1 in.) for height and 1.3 kg. (almost 3 lb.) for weight. The previously observed trend of an increasing difference with age is again evident.

There remain for consideration three studies that afford comparison between the indigent and the wealthy classes. These studies were made in New York by Freeman,[18] Boas,[19] and Hellman.[20]

Freeman collected height and weight data at an orphanage and in his private medical practice. The orphanage sample comprised approximately 450 children [21] between 7 and 10 years of age measured at "the Roman Catholic Orphan Asylums of New York." His other sample, not specified for size within the period 7 to 10 years, was part of a series of 278 "well-cared-for children" ranging in age from birth to 12 years.

TABLE 4.—*Body Size and Socioeconomic Status of North American Boys Seven to Ten Years of Age: Differences Between Means for Boys Admitted to Orphanages (O) and Those Receiving "Private" Health or Educational Guidance (P)*

Investigation	Difference, Mean of P Minus Mean of O			
	7 Yr.	8 Yr.	9 Yr.	10 Yr.
	Height, Cm.			
Freeman (1914) *	7.6	6.7	9.0	8.1
Boas (1923)	7.2	6.9	7.2	7.0
Hellman (1923)	7.0	7.5	8.2	8.9
	Weight, Kg.			
Freeman (1914) *	2.7	4.1	4.7	4.4
Hellman (1923)	2.3	2.5	2.9	2.6
	Number of Subjects			
Freeman (1914)				
Private practice †	?	?	?	?
Orphanage	110 ‡	110 ‡	110 ‡	110 ‡
Boas (1923)				
Private school §	?	?	?	?
Orphanage	250 ‡	220 ‡	165 ‡	150 ‡
Hellman (1923) ‖				
Private practice	11	17	24	26
Orphanage	48	70	82	79

* Children of both sexes.
† Part of a series of 278 children under pediatric guidance for varying periods between birth and 12 years.
‡ Approximate number.
§ Boas stated only that "a considerable number" of subjects was used.
‖ Some boys may have been included in both the Boas and the Hellman samples.

Boas analyzed data for height on private school and orphanage boys. The former were secured from measurement of "a considerable number of boys of Jewish descent in expensive private schools," and the latter, from measurement of about 750 orphan boys at the time of their admission to the Hebrew Orphan Asylum or the Hebrew Shelter and Guardian Society. The orphanage data were accumulated over the years 1905 to 1922; Boas did not state when the private-school materials were gathered.

18. Freeman, R. G.: Weights and Measurements of Infants and Children in Private Practice Compared with Institution Children and Schoolchildren, Am. J. Dis. Child. **8**:321-326 (Nov.) 1914.

19. Boas, F.: The Growth of Children as Influenced by Environmental and Hereditary Conditions, Sch. and Soc. **17**:305-308 (March 17) 1923; Studies in Growth, Human Biol. **7**:303-318 (Sept.) 1935.

20. Hellman, M.: Nutrition, Growth and Dentition, Dent. Cosmos **65**:34-49 (Jan.) 1923.

21. Freeman did not separate the sexes.

Hellman studied the height and weight of boys "from among the wealthy of New York" and "from among the poor of New York." The wealthy group was obtained in private orthodontic practice; it comprised Hebrew boys "brought up under the most favorable conditions." The poor group was secured at a Hebrew "orphan asylum."

Table 4 itemizes and aligns the results—the differences between the means for height and weight at successive annual ages—from each study. The mean of the 12 height differences is 7.6 cm. (3 in.) and the mean of the eight weight differences 3.3 kg. (7¼ lb.). To generalize that these means typify the average height and weight differences between North American boys at the extremes of the socioeconomic distribution appears hazardous. It is not improbable that Freeman's orphanage sample contained a larger proportion of children of southern European ancestry than his private-practice series, that the orphanage sample of Hellman contained a larger proportion of boys of eastern European ancestry than his private-practice series, or that the orphanage sample of Boas lacked both ethnic and secular comparability with his private-school series. Research is needed in which the racial and secular factors are shown to have been brought under reasonable control and in which the body sizes of children representing the extreme tails of the North American socioeconomic continuum are compared.

SUMMARY

A synthesis is given of present knowledge on the association between socioeconomic level and body size. The synthesis pertains to the period of middle childhood and to studies made in the United States and Canada.

Of the 12 studies utilized, 10 are drawn from the research literature on child growth and 2 are original. Systematic colligation for the age interval 7 to 10 years warrants the following generalizations:

North American boys representing the professional and managerial occupational groups average 1 in. taller and 3 lb. heavier than those representing the unskilled and semiskilled groups. There are similar differences between boys attending public schools in the best residential areas of large North American cities and those attending public schools in the poorest districts.

North American boys typifying the professional and managerial portion of the socioeconomic distribution exceed those typifying the unskilled and semiskilled portion not only in height and weight but also in girths of the trunk and limbs, breadths of the shoulders and head, and length of the extremities.

On the average the differences in body size between North American boys belonging to diverse socioeconomic groups are greater at 10 years than at 7 years. While the increase with age is small, it is manifested in practically all comparisons.

There is need for adequately controlled studies in which comparison of average body size is made for children typifying the extremes of the socioeconomic continuum. The information presently avaliable indicates that at the middle-childhood ages North American boys of the indigent class probably are more than 2 in. shorter and 5 lb. lighter than those of the wealthy class.

Case Reports

INFANTILE CORTICAL HYPEROSTOSIS (CAFFEY-SMYTH SYNDROME)

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IN THE year 1945 Caffey and Silverman [1] first described a new syndrome which they called "infantile cortical hyperostosis." At about the same time Smyth, Potter, and Silverman [2] reported independently a group of cases with similar changes under the title of "Periosteal Reaction, Fever and Irritability in Young Infants." Ross and Burke [3] suggested the name Caffey-Smyth for this new syndrome. It is a distinct clinical entity occurring in early infancy, usually before 3 months of age. It is characterized by a typical facial appearance, swelling of soft tissue, and roentgenographic changes in various bones, especially mandible, clavicles, scapulas, and ribs. Most of the cases have associated fever, anemia, and irritability. The etiology of the disease is obscure. The active manifestations subside completely after a variable period, usually within weeks, with no serious complications and no sequelae. The condition is now known to be not uncommon in pediatrics. We are adding two additional cases.

REPORT OF CASES

CASE 1.—N. D., age 3 months, was admitted to the Maimonides Hospital on April 24, 1941, with a three weeks' history of irritability and swelling of the right side of the face and neck and inability to move the right upper extremity.

Family History.—Both parents were alive and well. There was no history of familial or hereditary diseases.

Past History.—The baby was delivered at full term by low forceps after 15½ hours of active labor. The prenatal and pregnancy history had been normal. The birth weight was 8 lb. (3,600 gm.). The child was born in good condition. He was breast fed for three weeks and then received an evaporated-milk formula. Because of loose stools it was changed to whole milk. At the time of admission he was also getting cereal, orange juice, and 12 minims (0.74 ml.) of percomorph liver oil.

Present Illness.—Three weeks before admission, the infant had a rise in temperature and was irritable and the condition was diagnosed as "grippe." Two days later, the mother noticed swelling of the right cheek and the condition was now diagnosed as "swollen glands." A few days later, swelling of the left cheek was noticed and the eyes appeared puffed. The fever persisted, and a week after onset of illness the child was unable to move the right upper extremity.

From the Pediatrics Department of the Maimonides Hospital.

1. Caffey, J., and Silverman, W. A.: Infantile Cortical Hyperostoses: Preliminary Report on a New Syndrome, Am. J. Roentgenol. **54**:1-16 (July) 1945.

2. Smyth, F. S.; Potter, A., and Silverman, W. A.: Periosteal Reaction, Fever and Irritability in Young Infants: A New Syndrome? Am. J. Dis. Child. **71**:333-350 (April) 1946.

3. Burke, F. G., and Ross, S.: Infantile Cortical Hyperostoses (Caffey-Smyth Syndrome): Case Report, Clin. Proc. Child. Hosp. **4**:139-147 (May) 1948.

Physical Examination.—Examination revealed an obese, well-developed, pale infant of about 3 months of age with a marked swelling of the lower part of the face. The child seemed very irritable, especially on palpation of the involved parts. The head appeared normal in size and shape. The anterior fontanel was open, and the posterior fontanel was closed. The conjunctivas were pale; the pupils reacted to light. The ears were normal. The face appeared full and revealed a brawny induration of the right mandible extending from the lobe of the ear to about the middle of the chin. The child had no difficulty opening his mouth, and the mucous membrane was clear. The tongue was moist and clear. The pharynx appeared normal. There was no rigidity or visible deformity of the neck. A fulness was noted over the right upper chest, and a marked induration of the right clavicle was felt, especially over the inner two-thirds. The rest of the examination gave essentially negative results.

Laboratory Data.—The hemoglobin ranged between 7.65 and 8.5 gm.; the red blood cell count varied from 2,700,000 to 3,500,000; the total white blood cell count ranged between 13,000 and 27,600, with a normal differential count for the age. Examination of the blood smear revealed achromia, anisocytosis, and poikilocytosis. Urinalysis, including Bence-Jones tests,

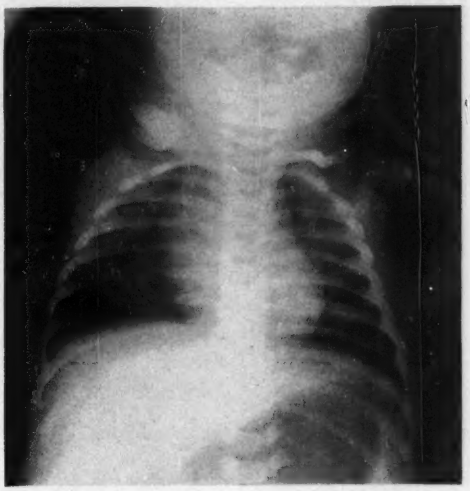

Fig. 1 (Case 1).—Bilateral pronounced thickening of mandible.

showed nothing abnormal. Blood chemistry studies revealed the following: the plasma calcium varied between 8.7 and 12.5 mg. per 10 cc., and the phosphorus ranged between 3.0 and 3.7 mg. per 100 cc. Blood cultures showed no growth. Wassermann and tuberculin reactions were negative. Vitamin C content of the blood was 1.2 mg. per 100 cc.

Roentgen Report.—The mandibular thickening was bilateral and pronounced (Fig. 1). The inner half of the right clavicle was completely replaced by a homogeneous opaque shadow which blended with that surrounding the outer half of the clavicle (Fig. 2). The right scapula showed similar changes. The eighth left rib showed slight periosteal changes. The cranial vault, sinuses, and occiput were normal. The rest of the bones were normal. A roentgenogram taken of the clavicles and scapulas 10 days before admission was essentially normal.

Biopsy.—With the patient under local 1% procaine hydrochloride anesthesia, a portion of bone and periosteum were removed. The periosteum appeared thickened, but the cortex appeared normal. No abnormal amount of bleeding was encountered.

Pathological Report.—The specimen consisted of four small spicules of spongy bone and four minute bits of soft hemorrhagic tissue. The microscopic section showed striated muscle

surrounded by and mixed with young dense fibrous connective tissue and fat. The bony spicules were made up of bony lamellas, the marrow spaces of which were filled mainly with a fibrillar layer containing fibroblasts and capillaries. The diagnosis was fibrosing osteitis.

Differential Diagnosis.—The lesions involving the right mandible, clavicle, scapula, and rib were considered to be either inflammatory or neoplastic in origin. The flaccid paralysis was thought to be due to the bone lesion. Syphilis, scurvy, neuroblastoma, or hyperparathyroidism were considered as possible causes of the condition.

Course.—Throughout the three-weeks' stay, the child was irritable and restless and had an irregular temperature. Besides the bony involvement of the mandible and right clavicle, the child had an infiltration of the right scapula. The flaccid paralysis of the right arm showed no improvement. He was given large doses of vitamin C and a transfusion of blood for the anemia. The weight on admission was 14 lb. 11 oz. (6,700 gm.) and on discharge was 18 lb. 4 oz. (8,300 gm.).

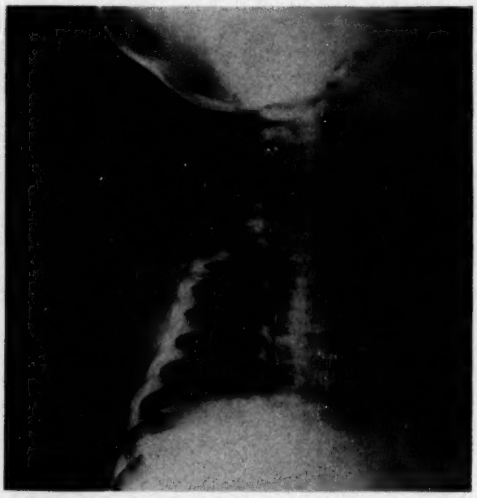

Fig. 2 (Case 1).—Involvement of right clavicle and right scapula. The eighth left rib shows slight periosteal changes.

Roentgenograms taken three months later at another hospital revealed practically complete healing of the bone lesions.

CASE 2.—A 3-months-old white boy was admitted to the Maimonides Hospital on Sept. 28, 1948, with a six weeks' history of gradually enlarging lower law, increasing irritability, pallor, and excessive salivation. The swelling of the jaw was not noticed by the family until called to their attention by others.

Family History.—The father was 28, the mother 22, and both were in good health. There had been no miscarriages or stillbirths. The father had infectious mononucleosis at 26. There was no history of bone disorders in either family.

Past History.—The baby was delivered at full term by forceps with much difficulty because of transverse position of the head. The birth weight was 8 lb. 14 oz. (4,000 gm.). There was no cyanosis. Slight jaundice developed during the first week of life. The child contracted impetigo while in the hospital, and this continued for two and one-half months. The infant received an evaporated-milk formula with supplementary orange juice and 15 minims (0.92 ml.) of percomorph liver oil. He had no difficulty in eating or swallowing.

Physical Examination.—Examination revealed a well-developed, well-nourished, white boy 3 months of age. He was very irritable. The circumference of the head was 41.5 cm., and the

anterior fontanel was open. The shape was normal, and there was no craniotabes. The child showed a peculiar facies and a moderate pallor (Fig. 3). There were slight protrusion of the eyes and slight edema of the lower lids. The mandible had a brawny induration from the lobules of the ears to the chin. There was marked thickening of both clavicles. The thickening and widening were felt in both scapulas and on some ribs on both sides. The involved areas were tender, with the greatest tenderness being over the ribs. The neck was short and thick, and the entire neck area was erythematous. The tongue was slightly enlarged. The mucous membrane of the mouth was normal. The throat was clear. The chest was well-developed. The circumference at the nipple line was 43 cm. The heart and lungs were normal. The abdomen was not distended. The liver and spleen were not palpable. There was a cherry-size, reducible umbilical hernia.

Laboratory Data.—The hemoglobin varied from 42 to 60% (6.1 to 9 mg. per 100 cc.) and the red blood cell count from 3,300,000 to 3,850,000. The white blood cell count varied from

Fig. 3 (Case 2).—Characteristic facial appearance.

16,500 to 29,600, and the polymorphonuclear cells varied between 40 and 58%, the lymphocytes between 35 and 59%, and monocytes between 1 and 7%. The thrombocyte (platelet) count was 546,000. The reticulocyte count showed 0.1%. The fragility test revealed beginning hemolysis at 0.46% and hemolysis completed at 0.34% NaCl. The urinalysis gave normal results. Blood chemistry studies revealed glucose 74 mg. per 100 cc., and total protein 5.38 mg. per 100 cc., of which 2.32 mg. was albumin and 3.06 mg. globulin. Total cholesterol was 190 mg. per 100 cc., of which 33% were esters. The serum calcium was 8.4 mg. per 100 cc., and the serum phosphorus was 5.6 mg. per 100 cc. The alkaline phosphatase was 33.6 Bodansky units. The carbon dioxide was 18 mEq. and the icteric index 7.8. The cephalin flocculation reaction was negative, and the thymol turbidity was 6.5. The vitamin C level of the blood was 0.6 mg. per 100 cc. of blood. The bleeding time was three minutes and coagulation time two and one-half minutes. The corrected sedimentation rate of the erythrocytes varied between 80 and 93 mm. in one hour. Blood cultures showed no growth. Blood agglutination tests for typhoid, paratyphoid A and B, brucellosis, and Proteus were negative. The Wassermann, Kahn, and Rosenthal serologic reactions were negative.

The Mantoux test gave a negative reaction. Bone-marrow study showed essentially normal results. The electrocardiogram tracing was within normal limits.

Roentgen Report.—Roentgenographic examination of the skeleton disclosed hyperostosis of the mandible, both clavicles, both scapulas, and several ribs on both sides (Fig. 4). The upper and lower extremities were normal. The most conspicuous changes were in the mandible and clavicles.

Diagnosis.—The diagnosis on admission was infantile cortical hyperostosis.

Course.—The patient remained in the hospital for three weeks. The weight gain was from 13 lb. (5,900 gm.) to 14 lb. 5 oz. (6,500 gm.). The temperature remained between 98 and 100 F., except for three occasions when it rose to 100.4 F. Irritability continued throughout the stay in the hospital. Pallor improved after transfusions of 150 cc. of whole blood on Oct. 1 and 18.

Fig. 4 (Case 2).—Involvement of both clavicles, both scapulas, mandible, and two ribs on right side.

He was discharged on Oct. 19, 1948, with the swelling of jaw, clavicle, scapulas, and ribs unchanged but with improvement in his general condition. A roentgenogram taken 16 months later and sent by his physician from California showed complete healing of his bone lesions (Fig. 5).

COMMENT

We observed the first patient in 1941. A thorough study, including a biopsy of the clavicle, shed no light on the case. It remained hidden in our files with an indefinite diagnosis. The second case was recognized by one of us (J. R.) from the characteristic facial appearance. The first case was then recalled, and a restudy revealed the true nature of the condition. Since the reports of Caffey and Smyth and their co-workers, the disease has become well known to pediatricians. The diagnosis of the condition is not difficult.

It appears to be a distinct clinical entity and occurs in children under 4 months of age, and in most cases the symptoms begin before the third month. It is characterized by irritability, fever, anemia, periosteal involvement of certain bones, and a characteristic brawny facial edema. The only case in a young infant without

mandibular involvement was the one reported by Delano and Butler.[4] The older cases reported by Caffey and Smyth are probably not part of this syndrome. They are most likely examples of hypervitaminosis A.[5] The facial appearance is so typical that a presumptive diagnosis can be made on inspection, as was done in our second case.

Fever was a prominent symptom in the first case but not in the second. Fever and irritability were prominent symptoms in most of the cases reported. Fever may have been overlooked in some cases because the patients were seen too late in the disease.

Pseudoparalysis of the right upper extremity was present in the first case. It was also observed by Caffey, Delano and Butler, Fink,[6] and Kane and Borzell.[7]

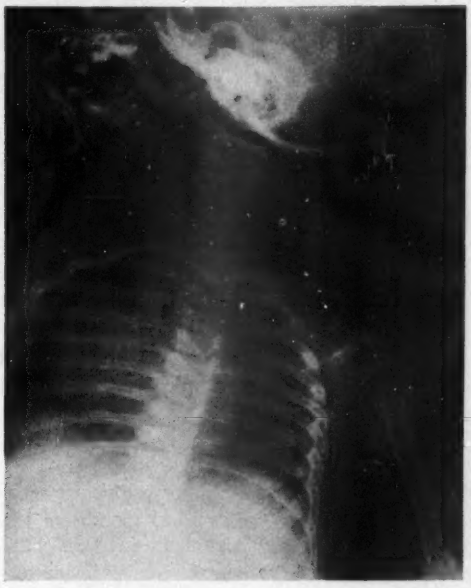

Fig. 5 (Case 2).—Complete healing of the bone lesions 16 months later.

Caffey thought that it might be due to birth injury to the brachial plexus. It is most likely due to infiltration of the scapulas, as all the patients with pseudoparalysis had scapular involvement.

Three of the four patients reported by Caffey had pleural effusion, and these revealed costal involvement. On the other hand, many of the patients reported,

4. Delano, P. J., and Butler, C. D.: Etiology of Infantile Cortical Hyperostoses, Am. J. Roentgenol. **58**:633-636 (Nov.) 1947.

5. Toomey, J. A., and Morissette, R. A.: Hypervitaminosis A, Am. J. Dis. Child. **73**:473-480 (April) 1947.

6. Fink, C.: Infantile Cortical Hyperostosis, J. Iowa M. Soc. **37**:529-532 (Dec.) 1947.

7. Kane, S. H., and Borzell, F. F.: Infantile Cortical Hyperostoses: Case Report, Am. J. Roentgenol. **58**:629-632 (Nov.) 1947.

including our two patients, had costal involvement without demonstrable pleural reactions.

The outstanding feature of this syndrome is the soft-tissue swelling and roentgenographic changes of the underlying bones. Soft-tissue swelling sometimes precedes the bone changes, as occurred in our first case. Some patients reveal neither visible nor palpable swelling, but changes are noted on routine roentgenographic study. The essential skeletal changes have been demonstrated to be a subperiosteal cortical hyperostosis causing external thickening of bone. The mandible has been involved in all cases but one.

Caffey and Smyth have noted the absence of mandibular involvement in patients with onset after the age of 11 months. These cases are most likely examples of hypervitaminosis A. Caffey in his first report questioned whether these cases were the same disease and now is convinced that the conditions in older children are unrelated to the disease in young infants.

The mandibular involvement gives the syndrome the characteristic facial appearance which allows one to make the diagnosis on first appearance. The other bones involved, in order of frequency, are the clavicles, ribs, scapulas, and long bones. The clavicles and ribs frequently show bilateral involvement. The scapula involvement is usually unilateral. Our second case and the one reported by Delano and Butler are the only two with bilateral scapular involvement.

Biopsies of various bones have been reported in a number of cases. Most of the reports, including our first case, showed a simple hyperplasia of the cortex. However, Kane and Borzell and Larkin and Rousseau [8] have reported evidence of inflammatory infiltration with periosteal hyperplasia.

The disease has a benign course. It is important to make the correct diagnosis in order to avoid unnecessary mutilating surgical procedure because of mistaken diagnosis of bone neoplasm.

SUMMARY

Two additional cases of infantile cortical hyperostosis are reported. The symptoms in both patients began before they were 3 months of age, and they both presented the typical bony involvement and characteristic facial appearance. The second patient presented the unusual bilateral scapular involvement. Both infants recovered completely.

161 Rugby Rd.

670 Ocean Ave.

8. Larkin, V. deP., and Rousseau, P.: Infantile Cortical Hyperostosis, Am. J. Dis. Child. **79**:105-111 (Jan.) 1950.

TRICHOBEZOAR

Discussion and Report of a Case

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AND
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MILWAUKEE

THE DIAGNOSIS of trichobezoar or hair ball in the stomach is frequently missed because it is seldom considered. The presentation of this case of trichobezoar in an 11-year-old girl is a reminder of its occasional occurrence and emphasizes the pitfalls in its diagnosis.

COMMENT

In 1938 DeBakey and Ochsner reviewed the world literature on the entire subject of bezoars. These authors noted that as early as the 12th century B. C. the Hindus believed in the healing powers of the bezoar stone from a goat's stomach, and until the 18th century bezoars were advocated for neutralizing poisons, destroying venoms, rejuvenating old people, and in treating epilepsy, dysentery, plague, and leprosy. The first reported case of trichobezoar has been accredited to Baudamant in 1779, although it was not until 1883 that the first report of a trichobezoar removed at surgery was published.[1]

Causes of hair swallowing (trichophagia) have been widely investigated. Animals with perverted appetites have been cured when missing dietary elements have been supplied.[2] It is probable that nutritional inadequacies contributed to the development of hair swallowing in these animals. This is not usually applicable in humans, but could conceivably play a role in some cases. Some persons with trichobezoars have associated abnormal cravings for unusual foods.[3] Two patients acquired the habit of hair swallowing during the delirium of typhoid.[4] Most observers agree that a definite underlying personality maladjustment exists in all cases.

It is well known that trichobezoars are found most commonly in girls and young women;[4] 91.4% of a series of 171 cases were noted to occur in women in the second decade of life.[1] Matas believes hair swallowing occurs predominantly in girls "solely because of the greater opportunity and temptation offered by the

1. DeBakey, M., and Ochsner, A.: Bezoars and Concretions: Comprehensive Review of the Literature with Analysis of 303 Collected Cases, and Presentation of 8 Additional Cases, Surgery **4**:934-963 (Dec.) 1938.

2. Schwartzman, J.: Trichobezoar, J. Pediat. **11**:691-696 (Nov.) 1937.

3. Sawyer, K. C.; Coppinger, W. R., and Nelson, J. M.: Trichobezoar in a 4-Year-Old Child, J. Pediat. **37**:393-395 (Sept.) 1950.

4. Bennett, D. E.: Recurrent Trichobezoar: Report of a Case, New England J. Med. **210**:307-309 (Feb. 8) 1934.

long hair of girls."[5] Studies on the factors responsible for the nonpassage of trichobezoars from the stomach or duodenum have thus far been inconclusive, although a diet of pasty foods may contribute.[1]

Clinically patients with trichobezoars appear surprisingly well and may live many years before symptoms are noted. Almost uniformly anorexia, weakness, malaise, and vague gastrointestinal complaints appear as presenting complaints. DeBakey and Ochsner noted a palpable abdominal mass in 87% and hematemesis in 6.1%.[1] Schwartzman emphasizes the frequency of an unhealthy and tired appearance and states that during sleep restlessness and tooth grinding may be noted.[2] Fever is conspicuously absent.

Laboratory studies may reveal secondary anemia and mild leucocytosis or may show no significant abnormality.

The two most essential diagnostic features are an accurate history of trichophagia and the demonstration of a mass within the stomach. Careful interrogation of the child may be helpful, but in most cases it is the parent who implicates the child as a hair swallower. Usually the child will deny any such tendencies. An almost classic remark was made by the patient in our report. The preoperative diagnosis had been missed by numerous doctors in several parts of the United States. After the operation for the removal of a trichobezoar, the patient quipped, "I could have told them I swallowed hair, but nobody asked me."

An intragastric mass may be demonstrated roentgenographically by air insufflation of the stomach.[1] Gastroscopic examination may provide a method of direct visualization of a trichobezoar,[6] but this procedure is usually not necessary. The most practical and reliable method is fluoroscopic visualization of the stomach during and after the administration of a barium meal.

The more important features of fluoroscopic examination are emphasized by DeBakey and Ochsner:

> Fluoroscopy is best performed with the patient in the upright position. Barium enters the cardia then stops temporarily in the region of the fundus. Suddenly it trickles or diffuses slowly down on either side of the non-opaque foreign body. Streaks or bands of barium then rapidly extend down, fuse, and finally reveal the entire stomach, normal in contour but apparently increased in size. By palpation a mass is seen to be freely movable and actually within the stomach. At the end of six hours most of the barium has left the stomach.[1]

Schwartzman notes that a hair ball which is not tightly packed produces a mottled gastric shadow.[2]

The only satisfactory treatment of trichobezoar is surgical removal. Regardless of the color of the patient's hair, trichobezoars are known to have a greenish-brown or black color at the time of removal. When the stomach is opened in the operating room, it is common to find extensions into the duodenum. Hurwitz emphasizes that a careful search be made for the presence of multiple hair balls at the time of operation.[7] The mortality in cases with operation is reported by various authors

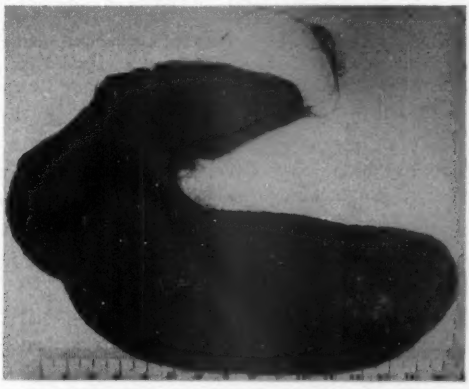
5. Matas, R.: Hair Balls, or Hair Casts, of the Stomach, and Gastrointestinal Tract, Tr. South. Surg. & Gynec. Assn. **27**:572-606, 1914; Hair Balls and Hair Casts of the Stomach and Gastrointestinal Tract, Surg., Gynec. & Obst. **21**:594-608, 1915.

6. Patterson, C. O., and Rouse, M. O.: Foreign Bodies in the Stomach Observed Through the Gastroscope: Report of 5 Cases, Texas J. Med. **36**:238-241 (July) 1940.

7. Hurwitz, A.: Trichobezoar, New England J. Med. **213**:721-722 (Oct. 10) 1935.

to be about 4%, and this figure has remained rather constant in the last three decades. The mortality in cases without operation is said to be 72.3%.[1] Ulcers are found at operation in 15% of cases of trichobezoar, and 80% of these ulcers are found on the lesser curvature.[1] Other complications include obstruction, perforation and peritonitis. Recurrences are not uncommon. Harris cites a case in which re-formed hair balls were removed from the stomach of a patient six times during a 13-year period.[8]

The weight of the trichobezoars varies. The specimen in our case weighed 2½ lb. (1,100 gm.) at the time of operation. The largest specimen obtained was probably one weighing 6½ lb. (2,900 gm.).[1] Distinction, however, must be made between "wet weight," obtained immediately after removal, and "dry weight," obtained after the specimen has dried for several days or more. In the latter case the weight of the specimen is reduced as much as 60%.



Trichobezoar weighing 2½ lb. removed from the stomach of an 11-year-old girl.

REPORT OF CASE

A. F., an 11-year-old white girl, complained of pain of one year's duration in the epigastric region. This distress was first noted after a mild attack of varicella. The child experienced paroxysms of sharp abdominal pain in the midepigastric region lasting up to one and one-half hours and occurring several times a month. The girl could obtain partial relief by flexing her legs on her abdomen and flexing her spine. No associated history of trauma, bleeding, or ecchymotic tendency was noted. The girl had suffered from chronic anorexia. The child's mother had been instructed by a pediatrician to give small, frequent feedings. The stools were of normal color, consistency, and frequency.

The child had been delivered by Caesarean section after an uneventful pregnancy. Jaundice was present at birth, lasted for seven days, but did not recur. Measles, mumps, and chicken pox occurred during early childhood. A tonsillectomy was performed when the girl was 8 years old.

The family history revealed that the girl's father and one brother had seasonal hay fever and asthma. No other significant data were learned.

Physical examination showed a well-developed, fairly well-nourished white girl. The head, eyes, ears, nose, pharynx, neck, thorax, lungs, and heart were normal. Palpation and percussion of the abdomen revealed a firm, smooth, slightly tender mass in the epigastric region, extending

8. Harris, R.: Recurrent Hair Ball of the Stomach, Lancet **2**:1006 (Nov. 21) 1925.

beneath the costal border from the left midclavicular line to the right parasternal line and extending inferiorly to approximately 4 cm. above the umbilicus. No other physical findings were recorded.

Urinalysis showed all values normal. The red blood cell count was 4,200,000 per cu. mm. The hemoglobin was 13.5 gm. per 100 cc. The white blood cell count was 12,150 per cu. mm.

Previous study had included multiple examinations and consultations by numerous physicians and clinics in several different medical centers. Complete records from all these are inaccessible. Roentgenographic studies of the gastrointestinal tract with barium (but without fluoroscopy) were reported to show normal emptying time for the stomach. Complete hematological studies disclosed no abnormality. Diagnoses of idiopathic splenomegaly, splenomegaly of undetermined origin (Banti's disease), or gastric carcinoma were made by different physicians. Exploratory surgery was then elected, and the girl entered the Sarah Morris Hospital for Children in Chicago, in the surgical service of Dr. Alfred Strauss.

With the patient under general anesthesia, a left rectus incision was made. When the abdomen was opened, an unattached hard mass was found, making a complete case of the stomach. The stomach was opened by a longitudinal incision on the anterior wall. A mass of hair was found; this had the complete form of the stomach and was "rock-like." The spleen, kidneys, and intestines appeared normal.

The specimen removed is shown in the illustration. The pathological report indicated that the specimen was a hook-shaped mass of matted and intertwined hair coated with thick mucus, measuring 14 by 8 cm. along each extremity. The weight of the specimen at the time of removal in surgery was 2½ lb.

SUMMARY

A case of trichobezoar in an 11-year-old girl is presented.

A reminder is given of the occasional occurrence of cases of trichobezoar in the stomach.

A brief discussion of historical points of interest, causative factors, incidence, and clinical manifestations is presented.

The diagnosis of this condition is considered, with special emphasis on the importance of an accurate history and the fluoroscopic examination.

IDIOPATHIC ACQUIRED HEMOLYTIC ANEMIA IN AN INFANT

Successful Treatment with Corticotropin (ACTH)

LIEUTENANT (jg) JOHN F. MEYER (MC), U.S.N.R.

DEVELOPMENT of new techniques has revived interest in the hemolytic anemias and has led to new concepts in the pathogenesis and treatment of the so-called idiopathic acquired form of the disease. Whereas treatment formerly was confined to the use of whole-blood transfusions, with unfavorable results occurring in many cases, recently splenectomy and corticotropin (ACTH) have been employed to induce remission.[1]

It is the purpose of this report to present a case of idiopathic acquired hemolytic anemia in an infant who failed to respond to repeated blood transfusions but recovered after treatment with corticotropin.

REPORT OF CASE

T. B., a white boy 13 months of age, was admitted to the Medical Service of Milwaukee Children's Hospital on July 1, 1950, because of vomiting, pallor, and weakness.

The infant had been well until June 15, 1950, when a "cold" developed. Within a few days recovery occurred, and the mother noted no unusual signs until June 29, when he became irritable and would not eat. During the next 48 hours he showed increasing weakness and loss of "pep." Vomiting followed whenever formula was offered. On the morning of the day of admission the mother noted that the infant's skin was jaundiced and that his urine was pink.

The past medical history was not remarkable. The infant had never been sick and had not been immunized. The birth history was normal. The mother knew of no contact that the infant might have had with noxious agents; the only medication given for the respiratory infection had been a simple cough syrup.

The family history was negative for jaundice or any known blood disease in the mother, father, and brother. None of the maternal or paternal relatives had jaundice or anemia.

Physical examination revealed an irritable, blond, slightly jaundiced, one-year-old infant weighing 22 lb. (10,000 gm.). The rectal temperature was 101 F. The lips, buccal mucosa, and nail-beds were pale, but there were no petechiae. The pharynx was hyperemic. The liver, spleen, and peripheral lymph nodes were not enlarged.

Laboratory studies revealed a hemoglobin level of 3.0 gm. per 100 cc., an erythrocyte count of 1,300,000 per cu. mm., and a leucocyte count of 3,540 per cu. mm. The differential leucocyte count was neutrophilic metamyelocytes 2%, nonsegmented neutrophiles 5%, segmented neutrophiles 46%, lymphocytes 44%, and monocytes 2%. There were 29 nucleated red blood cells per 100 leucocytes. Thrombocytes (platelets) were 364,000 per cu. mm. The erythrocyte sedimentation rate (Westergren) was 174 mm. in one hour. The serum Kline reaction was negative. The serum icterus index was 20. The van den Bergh test gave an indirect but not a direct

From the Medical Service of Milwaukee Children's Hospital.

1. (*a*) Mitchell, A. G., and Nelson, W. E.: Mitchell-Nelson Textbook of Pediatrics, edited by W. E. Nelson, ed. 5, Philadelphia, W. B. Saunders Company, 1950, p. 1122. (*b*) Blackfan, K. D., and Diamond, L. K.: Atlas of the Blood in Children, New York, Charles Scribner's Sons, 1944, pp. 74-76. (*c*) Dameshek, W., and Schwartz, S. O.: Acute Hemolytic Anemia (Acquired Hemolytic Icterus, Acute Type), Medicine **19**:231, 1940. (*d*) Dameshek, W.; Rosenthal, M. C., and Schwartz, L. I.: The Treatment of Acquired Hemolytic Anemia with Adrenocorticotropic Hormone (ACTH), New England J. Med. **244**:117, 1951.

reaction. Urinalysis revealed a trace of albumin and acetone and a 1+ reaction for acetoacetic acid. The urinary sediment contained occasional granular casts but no red cells. Fecal urobilinogen was considerably increased above normal.

Treatment consisted in transfusion of 500 ml. of whole blood in aliquots of 250 ml. over a period of two days. By the third hospital day clinical recovery was almost complete. Laboratory determinations on July 6, the day of discharge, revealed normal erythrocyte count and hemoglobin level; a leucocytosis of 12,600 per cu. mm. and a sedimentation rate of 25 mm. in one hour persisted.

The infant was readmitted on July 12, six days after discharge, because of vomiting. The mother stated that he had seemed well for three days, and then symptoms identical to those of the first admission had developed. Pink urine was passed on the morning the infant was brought to the hospital.

Careful history taking again failed to reveal pertinent information.

Physical examination upon admission to the hematology service was essentially as before. The patient was irritable and pale. The skin had a faint lemon-yellow tint. There was no purpura or enlargement of lymph nodes, spleen, or liver.

Admission laboratory tests revealed a severe hemolytic anemia. The hemoglobin was 5.0 gm. per 100 cc. The erythrocytes numbered 2,100,000 per cu. mm., the leucocytes 19,600 per cu. mm., and the thrombocytes 374,000 per cu. mm. The differential leucocyte count was segmented neutrophiles 39%, lymphocytes 50%, monocytes 10%, and eosinophiles 1%. Forty-six nucleated red blood cells were seen per 100 leucocytes. Many spherocytes and polychromatophilic erythrocytes were in the stained blood smears.

Bleeding, coagulation, and clot-retraction times were normal, but the osmotic fragility of the patient's erythrocytes was greatly increased.[2] A direct Coombs test showed positive results.[3] Analysis of a 24-hour urine specimen for lead, suggested by one consultant, revealed 0.105 mg. per liter—well within normal range.[4]

Marrow aspiration was performed; the marrow was hyperplastic with inversion of the myeloid-erythroid ratio because of extreme normoblastic erythropoiesis.

Clinical improvement with return to normal erythrocyte and hemoglobin levels followed administration of whole-blood transfusions, but the effect was transient. Within a few days it became apparent from the rapid fall in erythrocytes and hemoglobin that transfused red cells were also being destroyed.[5] Repetition of the Coombs test, using the technic of Evans and Duane, showed agglutination in a titer of 1:32.[6]

Unfortunately, it was not possible to perform inagglutinable erythrocyte counts.[7] The antibody was identified as an autoagglutinin. It was possible to elute the agglutinin from a saline suspension of the patient's cells onto homologous red cells, thereby obtaining a positive indirect Coombs reaction.[8]

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2. Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, ed. 11, New York, W. B. Saunders Company, 1948, p. 214.

3. Coombs, R. R. A.; Mourant, A. E., and Race, R. R.: Detection of Weak and "Incomplete" Rh Agglutinins: A New Test, Lancet **2**:15, 1945.

4. Aub, J. C.; Fairhall, L. T.; Minot, A. S., and Rezinkoff, P.: Lead Poisoning, Baltimore, Williams & Wilkins Company, 1926, pp. 7-14.

5. Mollison, P. L.: The Survival of Transfused Erythrocytes, with Special Reference to Cases of Acquired Hemolytic Anemia, Clin. Sc. **6**:137, 1947.

6. Evans, R. S., and Duane, R. T.: Acquired Hemolytic Anemia: The Relation of Erythrocyte Antibody Production to Activity of the Disease: The Significance of Thrombocytopenia and Leukopenia, Blood **4**:1196, 1949.

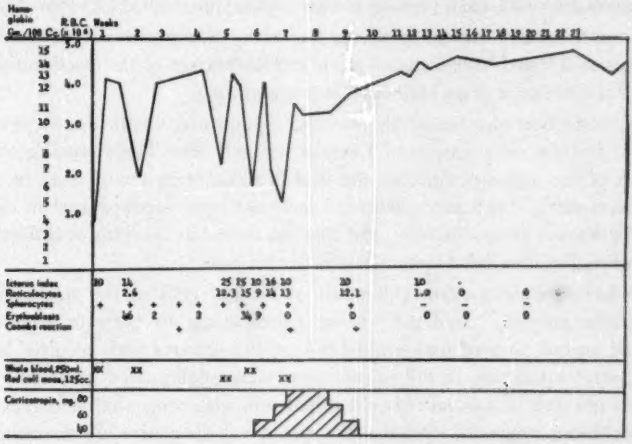
7. De Gowin, E. L.; Sheets, R. P., and Hamilton, H. E.: Studies with Inagglutinable Erythrocyte Counts: A Method for Measurement of Net Gain or Deficit of Red Cells in the Human Subject, J. Clin. Invest. **29**:693, 1950.

8. (*a*) Gardner, F. H.; McElfoesh, A. E.; Harris, J. W., and Diamond, L. K.: The Effect of Adrenocorticotropic Hormone (ACTH) in Idiopathic Acquired Hemolytic Anemia as Related to the Hemolytic Mechanisms, J. Lab. & Clin. Med. **37**:444, 1951. (*b*) Gardner, F. H.: Transfer to Normal Red Cells of an Agglutinin Demonstrable in the Acidified Sera of Patients with Acquired Hemolytic Jaundice, J. Clin. Invest. **28**:783, 1949.

After three weeks of replacement transfusion therapy, donor cells were still being destroyed almost as fast as they were given. The patient's condition was precarious. Splenectomy was considered, but it was decided to postpone operation pending a therapeutic trial of corticotropin.[9]

Treatment was begun with a daily dose of 20 mg. of corticotropin (Armour) administered subcutaneously every six hours. Over a period of five days the dose was gradually increased to 80 mg. daily; at this level circulating eosinophile counts were reduced to zero, and clinical response was noted.[10] A total of 450 cc. of red cell mass was also given during the first three days of corticotropin administration. The effect of the transfusions was to increase hemoglobin levels from 4.0 gm. to 9.5 gm. per 100 cc. and erythrocyte counts from 1,500,000 to 3,200,000 per cu. mm.

The large doses of corticotropin were continued for eight consecutive days. Appearance of puffy, moon-like facies, generalized edema, and a change in the patient's personality were considered indications for a gradual reduction in the daily level of corticotropin. Treatment was discontinued 10 days later.



Record of patient's cause; figures for reticulocytes and erythroblasts are percentages.

The patient's clinical course, after effective dosage of corticotropin was attained, was one of progressive improvement. Intravascular hemolysis ceased within a short time, as evidenced by a return to normal in reticulocyte counts and in the icterus index, together with disappearance of spherocytes and normoblastemia. Osmotic fragility of the patient's erythrocytes was almost normal when the test was performed two days before his discharge. Erythrocyte and leucocyte levels improved, but fall in autoagglutinin levels was very slow; a positive Coombs reaction was obtained up to the last hospital day.

Corticotropin was given over a period of 22 days. After cessation of therapy the patient was held in the hospital two additional weeks to allow continued observation. No clinical or laboratory evidence of hemolytic anemia was detected. The patient was accordingly discharged on Sept. 16 in complete clinical and hematological remission.

9. Dameshek, W.; Saunders, R. H., and Zannos, L.: The Use of ACTH in the Treatment of Acute and Subacute Leukemia, Bull. New England M. Center **12**:11, 1950.

10. Thorn, G. W.; Forsham, P. H.; Brunty, F. T., and Hills, A. G.: Test for Adrenal Cortical Insufficiency: Response to Pituitary Adrenocorticotropic Hormone (ACTH) in Man, J. A. M. A. **137**:1544 (Aug. 21) 1948.

Follow-up studies at weekly, and later, at monthly, intervals have shown no tendency for the anemia to recur. The Coombs reaction became negative by Jan. 2, 1951; all other peripheral blood tests showed normal results. When the patient was last seen, on April 6, 1951, his health was excellent.

COMMENT

The criteria for the diagnosis of acute hemolytic anemia may be summarized as including the following: chronic anemia, increased fecal urobilinogen, reticulocytosis, increased red cell fragility, and a normoblastic hyperplasia of the bone marrow.[11] The relationship of the spherocytes to hemolytic anemia[12] provides another important aid in diagnosis. These criteria have been fully met in this case.

Having made the diagnosis of acute hemolytic anemia, there still remains the differentiation between the congenital and acquired forms of the disease. Studies in the pathogenesis of these entities, however, have provided more accurate means of differentiation and have pointed toward successful methods of therapy.

Various causative factors in the pathogenesis of acute hemolytic anemia have been suggested[13] and have included stasis and destruction of the blood in the splenic pulp and the presence of an antibody (autoagglutinin).

The production of a hemolytic process in guinea pigs with use of serum from rabbits[14] and the development of Coombs serum[15] have made possible the determination of the autoagglutinin as the causative factor in many cases of acquired hemolytic anemia. Such autoagglutinins have not been demonstrated in congenital hemolytic anemia as conclusively, and this has served as a means of differentiation. Such autoagglutinins were demonstrated in this case.

The factor of destruction and stasis of the red cells in the spleen is also of considerable interest. Studies[15b] using splenic pulp of patients with acquired hemolytic anemia showed that washed red cells of patients with acquired hemolytic anemia, after incubation in the splenic pulp, were agglutinated by Coombs serum. This was not true of washed red cells of patients with congenital hemolytic anemia. The conclusions suggested were that the spleen was the source of the autoagglutinin which caused the red cells to be agglutinated by Coombs serum. The success of splenectomy in refractory cases has substantiated these studies somewhat. However, splenectomy in some cases does not bring about a favorable response, suggesting the role of some organ of the reticuloendothelial system.

Splenectomy was considered in this case. However, recent reports[16] on the use of corticotropin with favorable results deterred us from this decision. These reports

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11. (*a*) Boorman, K. E.; Dodd, B. E., and Loutit, J. F.: Hæmolytic Icterus (Acholuric Jaundice) Congenital and Acquired, Lancet **1**:812, 1946. (*b*) Kaplan, E., and Zuelzer, W. W.: Familial Nonspherocytic Hemolytic Anemia, Blood **5**:811, 1950. (*c*) Dameshek and Schwartz.[1c]

12. Dameshek, W., and Schwartz, S. O.: Hemolysins as the Cause of Clinical and Experimental Hemolytic Anemias, Am. J. M. Sc. **196**:769, 1938.

13. Dameshek, W., and Miller, E. B.: Pathogenetic Mechanisms in Hemolytic Anemias, Arch. Int. Med. **72**:1 (July) 1943. Footnotes 1*c*, 11*a*, and *b*.

14. Dameshek and Schwartz.[12] Dameshek and Miller.[13]

15. (*a*) Evans and Duane.[6] (*b*) Waglely, P. F.; Shen, S.; Gardner, F. H., and Castle, W. B.: Studies on the Destruction of Red Blood Cells, J. Lab. & Clin. Med. **33**:1197, 1948.

16. Dameshek, Rosenthal, and Schwartz.[1d] Gardner, McElfoesh, Harris, and Diamond.[8a]

suggested the effect of corticotropin as being dependent on a disruption of agglutinin production, presumably by regression of lymphoid tissue in which agglutinin may be produced. A trial of corticotropin was decided upon for this patient, and we were able to demonstrate a similar complete remission with a reversal of the Coombs reaction.

SUMMARY

A case history is presented of an acquired acute hemolytic anemia which became refractory to transfusion therapy.

A 22-day course of corticotropin was given in doses ranging from 40 to 80 mg. a day divided into six-hour intervals.

The response to treatment with corticotropin now represents a remission of seven months, including a reversal of the Coombs reaction.

A brief discussion of the pathogenesis and its relationship to this case is presented.

Abstracts from Current Literature

Biochemistry; Bacteriology and Pathology

A New Use for Mesomucinase. G. Salvioli, Clin. pediat. **32**:703 (Dec.) 1950.

Mesomucinase acts to dissolve the capsule of bacteria. A diffusing vaccine has been made from tubercle bacilli, killed by heat, with mesomucinase added to dissolve the capsule; this treatment should increase the potency of the vaccine; the vaccine may be dried and preserved for a long time. No clinical results are reported.

Higgins, Boston.

Metabolism; Infant Feeding; Milk and Other Foods

Amino Acid Supplementation of Proteins and Protein Hydrolysates. Henry S. Wyzan, Charles F. Kade Jr., and Jessy R. Shepherd, J. Nutrition **41**:347 (July 10) 1950.

From their data, Wyzan, Kade, and Shepherd found that the addition of large amounts of methionine, but not similar quantities of cystine, cysteine, alanine, glycine, phenylalanine, tyrosine, leucine, and choline, produced toxic symptoms and negative nitrogen balance in dogs. These experiments demonstrated that the addition of up to 40 mg. of nitrogen per kilogram of body weight as methionine enhanced nitrogen retention. Doubling the methionine supplementation not only threw the dogs drastically and suddenly out of balance but quickly caused deterioration of their physical condition. The apparent toxicity of methionine at these higher levels were severe enough to threaten death to the dog. It was apparent that the animal receiving these high methionine supplements was unable to utilize amino acids properly, even though they were fed in amounts which were ample for normal needs. The toxic effect of methionine-induced imbalance cannot be directly ascribed to its labile methyl group or sulfur content.

Fredeen, Kansas City, Mo.

The Arginine and Histidine Content of Meats. R. J. Sirny, I. T. Greenhut, and C. A. Elvehjem, J. Nutrition **41**:383 (July 10) 1950.

Sirny and associates determined by microbiological analyses with use of three different organisms the arginine and histidine content of 55 different samples of beef, pork, lamb, and veal muscle cuts and beef organs. Values for arginine in meats range from 6.1% of the crude protein in beef brain to 6.7% in beef heart. For histidine the values ranged from 2.5% in beef brain, kidney, and tongue to 3.4% in beef muscle. Retention of arginine during the roasting of meats ranges from 94 to 107%; while that of histidine ranges from 79 to 101%.

Fredeen, Kansas City, Mo.

The Effect of Phytate and Other Food Factors on Iron Absorption. Leon M. Sharpe, Wendell C. Peacock, Richard Cooke, and Robert S. Harris, J. Nutrition **41**:433 (July 10) 1950.

This present investigation was concerned with the effect of phytate—as contained (*a*) in rolled oats, (*b*) in a typical breakfast which included rolled oats, and (*c*) in sodium phytate—upon the absorption of radioactive iron in a group of adolescent boys. The results indicated that the phytate in rolled oats was relatively unavailable for the precipitation of food iron and that the solid content of the food may have an important effect upon the absorption of iron from the intestinal tract. The absorption of iron was greatest from the distilled water, presumably because it contained no interfering substances. Milk reduced iron absorption appreciably, almost as much as rolled oats. Since rolled oats and milk reduced absorption only twice as much as milk alone, it is possible that phytate was not an important factor in reducing the absorption of iron. Since the absorption of iron from water was approximately five times

greater than that from the breakfasts, it is apparent that medicinal iron administered in the morning before any food is eaten would be much more effective than iron taken with meals.

FREDEEN, Kansas City, Mo.

OBSERVATIONS OF AN UNKNOWN DIETARY FACTOR ESSENTIAL FOR HUMAN GROWTH. SELMA E. SNYDERMAN, L. EMMETT HOLT JR., ROSA LEE NEMIR, LOREN P. GUY, ROSARIO CARRETERO, and KATHERINE C. KETRON, J. Nutrition **42**:31 (Sept. 11) 1950.

A deficiency syndrome which occurs after prolonged feeding of a purified ration in which all the vitamins are supplied as synthetic supplements is described. The syndrome consists of a cessation of weight gain unaccompanied with any other symptoms or signs. A normal infant diet brings about an immediate weight gain; supplementation with brewer's yeast also has a beneficial effect after a preliminary lag period of 10 to 28 days. The existence of an unknown factor contained in the normal diet and necessary for human growth has been recognized. This factor may be identical with vitamin B_{12} or the "animal growth factor."

FREDEEN, Kansas City, Mo.

FURTHER STUDIES ON THE ROLE OF POTASSIUM IN GROWTH AND BONE FORMATION. M. B. GILLIS, J. Nutrition **42**:45 (Sept. 11) 1950.

In an otherwise adequate diet for maximum rate of growth during the first four weeks of life, chicks required 0.20% potassium. Because of an interrelation in the metabolism of potassium and phosphorus, the requirement for potassium was increased to as much as 0.24% when the phosphorus content of the diet was suboptimum. Bone calcification, as measured by the percentage of bone ash, was significantly influenced by the amount of potassium in the diet. Under such conditions the inorganic phosphorus in blood plasma was reduced, while there was no effect on the plasma calcium. The maximum feed efficiency was obtained with amounts of potassium optimum for growth. Results obtained with rats confirmed the effect of phosphorus on the potassium requirement for growth and bone calcification as observed in chicks. The potassium requirement of rats was approximately 0.16% of the diet. The amount of phosphorus required for maximum bone calcification in the rat was greatly in excess of the amount required for normal growth.

FREDEEN, Kansas City, Mo.

NUTRITIVE VALUE OF CANNED FOODS: XLII. A STUDY OF THE PROTEIN VALUE OF YOUNG AND MATURE PEAS (PISUM SATIVUM). R. G. CHITRE, J. N. WILLIAMS JR., and C. A. ELVEHJEM, J. Nutrition **42**:207 (Oct. 10) 1950.

It appears that canning does not decrease the biological value of nearly mature peas, while it enhances that of immature peas. Investigations concerning the cause of the poor biological value of immature raw peas suggest that hydrolysis of the protein and subsequent deamination of its amino acids occur through enzymatic action when the peas are moistened. Canning destroys the enzyme activity. The possibility is discussed that reactions during the drying process between the sugar in the raw peas and the amino acids freed by proteolysis contribute to the decrease in the biological value of the raw peas for the rat.

FREDEEN, Kansas City, Mo.

PROTEIN-BOUND IODINE IN INFANTS. T. S. DANOWSKI, S. Y. JOHNSTON, W. C. PRICE, M. MCKELVY, S. S. STEVENSON, and E. R. MCCLUSKEY, Pediatrics **7**:240 (Feb.) 1951.

Serum protein-bound iodine concentrations have been measured by the method of Barker, modified, in 154 serum samples from 110 term infants ranging in age from birth to 1 year. The mean value obtained within 12 hours of birth, 8.3 ± 2.4 γ per 100 cc., was indistinguishable from the mean for a group of 57 pregnant women including 13 of the mothers of the infants. During the remainder of the first week following birth a slight but statistically significant rise occurred in the protein-bound iodine of the serum samples. This subsequently disappeared. Beyond the 12th week of life the protein-bound iodine values fell in the 4 to 8 γ per 100 cc.

range characteristic of euthyroid older children and adults, but the mean concentration was significantly higher. Thyroxin measurements in eight of the infants revealed values considerably above those encountered in a group of euthyroid adults and even in excess of those seen during pregnancy.

These higher values in normal infants are presumably related to the growth and development during this period, particularly in view of the high thyroxin levels. These studies incidentally provide standards for early diagnosis of thyroid dysfunction hitherto unavailable for this age group.

FROM THE AUTHORS' SUMMARY.

ACTION OF ALLOXAN ON A HYPOGLYCEMIC INFANT. J. E. GRIFFITH JR., R. L. JACKSON, and R. G. JANES, Pediatrics **7**:616 (May) 1951.

A case report is presented of an 8-month-old white girl who had severe spontaneous hypoglycemia with associated convulsions. This condition was not appreciably improved with medical management, and a subtotal pancreatectomy gave only temporary relief. The administration of alloxan monohydrate caused a cessation of convulsions, elevated the blood sugar, and improved the glucose tolerance. The response noted in this child with alloxan therapy indicates that the initial dose should be approximately 55 mg. per kilogram of body weight, given by rapid intravenous injection. The dose should be increased by 5 mg. per kilogram of body weight daily until mild hyperglycemia is produced. Fourteen months after the last injection of alloxan, the child had remained free of convulsions and her social development age was considered to be within normal limits. Blood sugar values obtained during the 14-month interval were improved over the prealloxan picture. However, values below the normal fasting level have been observed.

FROM THE AUTHORS' SUMMARY.

GALACTOSEMIA IN INFANCY: REPORT OF A CASE WITH OBSERVATION FOR 24 MONTHS. J. W. DUSHANE and EVELYN E. HARTMAN, Pediatrics **7**:679 (May) 1951.

Galactose intolerance is a rare condition occurring in infancy. Characteristic features of the disease include lack of weight gain, emaciation, distention of the abdomen with enlargement of the liver and spleen, and, occasionally, formation of cataracts. Galactose and albumin are present in the urine. Elimination of galactose from the diet results in general improvement of the infant and disappearance of galactosuria and albuminuria.

A case of galactosemia in a baby aged 4½ months is described. Galactose was identified in the urine when the infant ingested milk, but no reducing substance was observed when milk was eliminated from the diet. The child appeared well, though small, and had no melituria for a 24-month period of observation on a milk-free regimen.

FROM THE AUTHORS' SUMMARY.

ACUTE NUTRITIONAL DISTURBANCE IN YOUNG INFANTS ASSOCIATED WITH MASTOIDITIS. C. E. SNELLING, D. E. S. WISEHART, and ALAN BROWN, Canad. M. A. J. **63**:563 (Dec.) 1950.

Attention is called to the so-called hidden mastoid infection in young children which may be the cause of nutritional disturbances characterized by vomiting, diarrhea, dehydration, and toxemia. In such cases mastoidectomy resulted in dramatic improvement. Fourteen cases are presented.

McGUIGAN, Evanston, Ill.

ASSESSMENT OF NUTRITIONAL STATUS OF SCHOOL CHILDREN IN LUCKNOW: PART I, PART II AND PART III. B. G. PRASAD, Indian J. Pediat. **16**:113 (July) 1949.

The nutritional status of 139 boys in Lucknow was assessed by 13 somatometric indexes and the "sacratama" index of von Pirquet. No somatometric index is considered satisfactory, and a clinical examination of every child is essential for the assessment of nutrition. Von Pirquet's index combines both somatometric and physical findings and is considered satisfactory.

McGUIGAN, Evanston, Ill.

ASSESSMENT OF NUTRITIONAL STATUS OF SCHOOL CHILDREN IN LUCKNOW: PART IV AND PART V. B. G. PRASAD, Indian J. Pediat. **16**:181 (Oct.) 1949.

The author continues his exhaustive study of school children. Part IV includes physical status as judged by direct observation (Hogarth's scale). The author considers that assessment of health by Sankaran's "defect score" is the best method. Knudsen and Schiøtz' sign of the dorsal median furrow was found to be a valuable supplementary assessment, and it is suggested that it might be included in the "defect" score card. No evidences of scurvy were found, though urinary excretion of vitamin C was low in a number of children. The percentage of Mantoux reactions which were positive showed a steady rise with age increase, with 83.4% giving a positive reaction at 13 to 14 years.

Part V comprises an inquiry into the incidence of clinical evidence of deficiency diseases, mottled enamel, and malocclusion of teeth in boys. Only one case of angular stomatitis and 11 cases of Bitot's spot were detected in 1,444 students. Incidence of mottled enamel was less than 10%. Malocclusion occurred in 34.1%.

McGUIGAN, Evanston, Ill.

NUTRITIONAL EDEMA. P. V. VEGHELYI, Ann. pædiat. **175**:349 (Nov.) 1950.

Fatty liver and edema which developed as a consequence of deficient feeding was studied in 109 infants.

Three stages could be discerned in the clinical course: one of pancreatic excretory failure, one of liver impairment, and one of edema. The condition did not respond to vitamins, but sufficient milk had a dramatic effect and small quantities of milk a deteriorating effect. Cases of purely nutritional origin soon reach the irreversible stage; fibrosis develops in the liver, and the patients are very susceptible to intercurrent infections.

The nature of the dietary factor responsible and the pathology of the disease are discussed in detail, and the conclusion is reached that a deficient diet inhibits the excretory activity of the pancreas and that it is this dysfunction which may lead to hepatic changes.

FROM THE AUTHOR'S SUMMARY.

THE IMPORTANCE AND STATE OF THE CIRCULATORY DISTURBANCE IN INFANT TOXICOSIS. KERPEL-FRONIUS, F. VARGA, I. KOVACH, and K. KUM, Ann. pædiat. **176**:11 (Jan.) 1951.

In 42 cases of toxicosis following diarrhea the causation and importance of the circulatory disturbance were investigated. Severity and prognosis are to a large extent dependent on the circulation time, on the difference in oxygen tension between the arterial and venous systems, and on the size of the minute volume; in short, on the intensity of the circulatory shock. The chief cause for the development of the anhydremia is the loss of between 25 and 30% of extracellular fluid; the increased capillary permeability contributes in some of the cases to the anhydremia. The basic symptoms of toxicosis — the mental disturbance, the acidosis, and the functional renal insufficiency — are the immediate sequelae of the circulatory shock and of the "stagnant" anoxia.

FROM THE AUTHORS' SUMMARY.

SPECIFIC DYNAMIC ACTION OF SOME AMINO ACIDS GIVEN TO CHILDREN BY MOUTH. A. DEGLI ESPOSTI, Clin. pediat. **31**:291 (May) 1949.

The basal metabolism was determined before and after 3 gm. of an amino acid was given to a child between 7 and 12 years of age; 13 amino acids were separately studied, 10 children being the subjects of the observations.

The metabolism showed an increase with each of the amino acids, varying from 7% with cystine to 14% with glycocoll. With 10 of the amino acids it was found that the higher the molecular weight of the amino acid, the lower the specific dynamic action. For three amino acids, histidine, tyrosine, and tryptophane, the specific dynamic action was somewhat higher than would be expected from their molecular weights. The specific dynamic action was not proportional to the percentage of amino nitrogen in the amino acid.

HIGGINS, Boston.

COMPOSITION OF FAT OF MILK OF MOTHERS WHOSE INFANTS ARE NORMAL. L. MARTONI, Clin. pediat. **32**:501 (Sept.) 1950.

As part of a study of the diet of infants with exudative diathesis, the author analyzed the fat of the breast milk of 12 mothers. The average fat content was 3.56%; of this, 53% was saturated fatty acids, 8% lanoleic acid, 0.5% linileic acid, and 38% oleic and other unsaturated acids.

HIGGINS, Boston.

SOLUTIONS FOR RELIEVING DEHYDRATED CHILDREN. MARGHERITA RICCARDI, Minerva pediat. **1**:258 (July) 1949.

Hypodermoclyses with the following solutions were given to normal children: 5% dextrose, isotonic sodium chloride, M/6 sodium lactate, 5% dextrose with M/6 sodium lactate, and isotonic sodium chloride with M/6 sodium lactate. Determinations of the hematocrit readings, the alkali reserve, and the cellular and serum chlorides of the blood were made before and after the clyses. On the basis of the data obtained, the proper treatment in three clinical cases is discussed.

HIGGINS, Boston.

Vitamins; Avitaminoses

A STUDY OF THE RELATION AND ADJUSTMENT OF BLOOD PLASMA LEVEL AND URINARY EXCRETION OF ASCORBIC ACID TO INTAKE. MARY L. DODDS, ECHO L. PRICE, and FLORENCE L. MACLEOD, J. Nutrition **40**:255 (Feb. 10) 1950.

In a study of the relation and adjustment of blood plasma level and urinary excretion of ascorbic acid to intake, Dodds and associates used 24 college women as subjects. Their data indicate that for the subjects of these experiments 75 mg. was adequate for maintenance, that an increase to 100 mg. was accompanied with an increase in urinary excretion, and that the retention was close to 1 mg. per kilogram of body weight, whether measured by reduced or total ascorbic acid.

FREDEEN, Kansas City, Mo.

ABSORPTION OF AQUEOUS DISPERSIONS OF VITAMIN A ALCOHOL AND VITAMIN A ESTER IN NORMAL CHILDREN. B. M. KAGAN, D. A. JORDAN, and P. S. GERALD, J. Nutrition **40**:275 (Feb. 10) 1950.

The purpose of this study was to determine whether it was the alcohol form of the vitamin as opposed to the ester form which was responsible for the more readily absorption of vitamin A. Kagan, Jordan, and Gerald concluded that it was the fact that it was in aqueous dispersion rather than in oil which was the important factor.

FREDEEN, Kansas City, Mo.

VITAMIN E CONTENT OF FOODS. PHILIP L. HARRIS, MARY L. QUAIFE, and WILLIAM J. SWANSON, J. Nutrition **40**:367 (March 10) 1950.

The richest dietary sources of vitamin E are certain of the vegetable oils. Cereal products and eggs are next in order of nutritional importance. Vegetables and animal products are rather poor sources of vitamin E. The value of cereal products as a source of vitamin E certainly depends upon the extent and severity of the milling process which they undergo prior to consumption.

FREDEEN, Kansas City, Mo.

SELF SELECTION OF DIET: XII. EFFECTS OF B VITAMIN DEFICIENCIES ON SELECTION OF FOOD COMPONENTS. E. M. SCOTT, ETHEL L. VERNEY, and PATRICIA D. MORISSEY, J. Nutrition **41**:373 (July 10) 1950.

This study by Scott and co-workers was of the effects of vitamin B deficiency on the choice by rats of casein, sucrose, fat, and salts and included an investigation of the relation of these choices to nutritional needs. The thiamine-deficient group selected more fat and less protein than the controls; the pyridoxine-deficient, less protein; and the pantothenate group, much less fat and more carbohydrate.

FREDEEN, Kansas City, Mo.

CONGENITAL ANOMALIES IN THE CHICK DUE TO VITAMIN B_{12} DEFICIENCY. ORLANDO OLCESE, J. R. COUCH, J. H. QUISENBERRY, and P. B. PEARSON, J. Nutrition **41**:423 (July 10) 1950.

Olcese and co-workers found that in hens fed a diet deficient in vitamin B_{12} there was a definite peak of embryonic mortality occurring at the 17th day of incubation. A myatrophy of the leg was the most characteristic symptom of deficiency present in the embryos; the legs were slender, about normal length and hemorrhagic in appearance. A malposition "head between the thighs" occurred frequently in eggs from hens deficient in B_{12}. Other anomalies were hemorrhages of the embryo and allantois and perosis.

FREDEEN, Kansas City, Mo.

THE PROTECTIVE ACTION OF VITAMIN B_{12} AGAINST THE TOXICITY OF DL-THYROXINE. BARNETT SURE and LESLIE EASTERLING, J. Nutrition **42**:221 (Oct. 10) 1950.

The ratio of vitamin to hormone was 0.3 to 200 γ; in other words, it took one part of vitamin B_{12} to protect against the toxicity of 666 parts of thyroid hormone, thyroxine.

FREDEEN, Kansas City, Mo.

AN UNKNOWN FACTOR WITH VITAMIN A ACTIVITY DISTILLED FROM LARD. HANS KAUNITZ and CHARLES A. SLANETZ, J. Nutrition **42**:375 (Nov. 10) 1950.

Lard contains a factor which has vitamin-A-like activity but is chemically different from the known forms of vitamin A. Molecular distillation of lard yields two fractions, the distillate of which possesses the capacity to counteract deficiency symptoms commonly considered the result of vitamin A deficiency. Young animals receiving 2% of the distillate in the diet and consuming about 5 to 8 gm. of food daily fared better than those receiving weekly supplements of 7.5 units of vitamin A palmitate.

FREDEEN, Kansas City, Mo.

GROWTH FAILURE IN SCHOOL CHILDREN AS ASSOCIATED WITH VITAMIN B_{12} DEFICIENCY: RESPONSE TO ORAL THERAPY. NORMAN C. WETZEL, W. C. FARGO, I. H. SMITH, and J. HELIKSON, Science **110**:651 (Dec. 16) 1949.

Vitamin B_{12} was given to 11 children, 5 to 12 years of age, under close supervision, in daily doses of 10 γ orally. All the subjects exhibited simple growth failure but no clinical evidence of vitamin B complex deficiency. One of the subjects is stated to be suffering from allergic bronchitis; specific disease as a cause for growth failure is not mentioned for the rest.

Five of the 11 subjects exhibited dramatic improvement, graphically portrayed by the Wetzel grid technique, to this single change in routine. The authors postulate functional B_{12} deficiency in this group.

FORBES, St. Louis.

SCURVY—RECENT EXPERIENCES. N. BARRIE COWARD, Canad. M. A. J. **63**:549 (Dec.) 1950.

The author analyzes 37 cases of severe clinical scurvy seen in five and one-half years. He points out the necessity of adequate vitamin C intake and emphasizes the need for the physician to make sure the child is getting the vitamin as ordered.

MCGUIGAN, Evanston, Ill.

THE EARLY DIAGNOSIS OF RICKETS. J. D. GRAY and F. STEPHEN CARTER, Arch. Dis. Childhood **24**:89 (Sept.) 1949.

An estimation of the plasma alkaline phosphatase level by the King-Armstrong method in 56 controls gives a range of 11 to 20 units, with an average of 17, for children between 1 month and 3 years of age. Over that age the average approximates to the figure for adults. In 64 cases of clinical rickets blood phosphatase levels were evaluated, many of them serially before and after treatment. The most frequent diagnostic titer lay between 25 and 40 units.

The prompt response to specific therapy is shown. The raised blood phosphatase level due to shock therapy has been noted and discussed. The phosphatase level in very early cases with symptoms but no signs averages 35 units.

The difficulties of diagnosis in borderline cases are mentioned, and it is suggested that a dose of calciferol, 200,000 units, followed by a further blood phosphatase estimation three weeks later may be of assistance in solving the problem. The difficulties of early roentgenological diagnoses are stressed, and it is suggested that the discrepancies which occur occasionally in cases of clinical rickets and a normal phosphatase level may be due to the persistence of physical signs in healed rickets.

KELLY, Milwaukee.

INFANTILE RICKETS. N. FELDMAN, South African M. J. **24**:1053 (Dec. 23) 1950.

The author reports the finding of many cases of rickets in all stages among the native infants in South Africa. He points out the fallacy of depending on ultraviolet irradiation from the sun and recommends routine fish liver oil addition to the diet.

McGUIGAN, Evanston, Ill.

HYPERVITAMINOSIS D_3. R. COMBE, Pediatrie **37**:542 (Sept.-Oct.) 1948.

In spite of previous publications warning against the dangers of overdosage of vitamin D_3, cases of hypervitaminosis seem to occur. The physician should be in a position to recognize early symptoms of hypervitaminosis in order to be able to use without danger large doses of vitamin D if they are indicated. The first symptom is sudden and severe anorrhexia, followed by nausea and vomiting. Urinary findings are polyuria, pollakiuria, and functional kidney disturbances, as demonstrated by various kidney function tests, such as dilution and concentration tests and intravenous urography. Nervous troubles vary in their manifestations (somnolence, asthenia, stupor, and others).

GLASER, Chicago.

OVERDOSAGE WITH VITAMIN A. G. MOURIQUAND, Presse méd. **56**:737 (Oct. 24) 1948.

Mouriquand points out that in experimental animals keratinization of epithelium, growth arrest, pulmonary lesions, and osseous dystrophy develop after they have received massive doses of vitamin A. Arctic explorers have been poisoned by eating liver from polar bears or seals, which is exceptionally rich in vitamin A.

It is advisable not to discredit the therapeutic use of vitamin A by the untoward symptoms caused by overdosage, as was the case with vitamin D preparations.

DAFFINEE, Melrose, Mass.

REPERCUSSIONS IN INFANT OF AVITAMINOSIS OF MOTHER DURING PREGNANCY. R. HOUET and SUZANNE LECOMTE-RAMIOUL, Ann. pædiat. **175**:378 (Nov.) 1950.

The authors present a description of a case with a multiplicity of signs indicating severe polyavitaminosis. For two years the patient's mother was fed in a D. P. camp a diet completely devoid of all vitamins. When the first girl was born, she was apparently normal, but she died at the age of 4 months from recurrent intestinal upsets. A second pregnancy was marked by particularly severe vomiting during the first few months. Shortly after the parents finally settled in Belgium, a boy was born with xerophthalmia in both eyes and a bilateral harelip. Vitamin A tests in the child's blood, vitamin B_2 examinations of the breast milk, and signs of early rickets proved a polyavitaminosis (A, B_2, D).

The author is of the opinion that the harelip was caused by the B_2 avitaminosis. In this connection the experiments of Warkany with mice are mentioned.

FROM THE AUTHORS' SUMMARY.

ACTION OF STREPTOMYCIN ON BLOOD LEVELS OF VITAMIN A. L. MARTONI and L. SALMI, Clin. pediat. **31**:653 (Dec.) 1949.

The vitamin A content of the blood was found to be consistently lower in children with tuberculous meningitis than in normal children. In both healthy and tuberculous children, streptomycin medication led to a higher vitamin A content in the blood.

HIGGINS, Boston.

VITAMIN D_3. C. IMPERATO and L. LEONARDI, Lattante **21**:617 (Oct.) 1950.

Vitamin D_3 (7-dihydrocholesterol) was given in massive doses of 250,000 units daily over periods of two to four days to nine infants with active rickets; several of the infants also had tetany. All the clinical and laboratory signs of tetany had disappeared within five days. Craniotabes had disappeared in 20 days. All the roentgenological signs of acute rickets had disappeared in 25 to 45 days.

HIGGINS, Boston.

HEPATIC LESIONS IN POISONING FROM VITAMIN D_2. C. ZUNIN, Minerva pediat. **2**:470 (Oct.) 1950.

Two cases of vitamin D poisoning in infants are reported; in each case the liver was enlarged, and in one a positive Takata-Ara reaction was found. The failure to find mention of liver disease in the literature in such cases led the author to study the effect of large doses of vitamin D_2 on rats. There was a typical steatosis of the liver in the rats when the vitamin was given either by injection or by mouth. The suggestion is made that signs and symptoms of hepatic involvement may be the first indications of vitamin D intoxication.

HIGGINS, Boston.

DETERMINATION OF VITAMIN B_2 IN THE URINE. ENRIQUE FERNÁNDEZ FLORES, MARGARITA JOHNSON, and MERCEDES GÓMEZ RIPPES, Rev. cubana pediat. **20**:580 (Oct.) 1948.

Observations were made on the urinary excretion of riboflavin of 34 persons, mainly adults. The direct fluorometric method of Najjar was used. The average amount of riboflavin excreted was 128.17 γ per liter of urine. In Germany persons given a normal diet excreted an average of 1,500 γ per liter of urine, and in the United States an average excretion of 700 γ daily was recorded.

The diet used was that generally used in Cuba, polished rice, little milk, little meat, frijoles, potatoes, white bread, crackers, and some fruit and varieties of root vegetables, boiled or fried.

KEITH, Rochester, Minn.

CURE OF RICKETS WITHOUT VITAMIN D TREATMENT BY FEEDING BOVINE SERUM. HANS E. REINLEIN and HELMUT H. GEERING, Arch. Kinderh. **138**:73 (Jan.) 1950.

Seriously ill infants were fed "Boviserin," a sterile bovine serum, digested for five to six hours with a pancreatic extract ("Pancreon") and mixed with a 12-to-15% gruel decoction of rice or barley. The albumin-globulin ratio of this protein mixture is similar to that of human milk albumin and it proved to be of high biologic value. In six infants, 7 to 15½ weeks of age, with florid rickets, who received this bovine serum mixture exclusively without addition of any other antirachitic therapy, a surprisingly prompt healing of the rickets was observed.

A rise of the euglobulin values was found in a few infants who were fed this serum mixture; this change in the blood proteins may explain the increased resistance to infections observed. No untoward reactions and no allergic phenomena were seen in 30 infants who received this bovine serum food.

ARON, Chicago.

VITAMIN D INTOXICATION IN CHILDREN. J. FLAMAND-CHRISTENSEN, Ugesk. læger **110**:625 (May 27) 1948.

The author reports six cases of vitamin D intoxication in children aged 4 months to 3 years. Four of the children had received 40,000 to 100,000 units of vitamin D daily for one to two and one-half months, and two children had received 1,000 to 2,000 units daily for several months. The symptoms and signs were typical. There were no deaths. The author draws attention to the marked individual variation in the tolerance of vitamin D. Sometimes, as in the latter two cases, signs of intoxication may be produced by moderate doses.

WALLGREN, Stockholm, Sweden.

Hygiene; Growth and Nutrition; Public Health

SOCIAL CAUSES OF DYSTROPHY. ALBERTO DUARTE GONZALEZ, Rev. chilena pediat. **22**:69 (Feb.) 1951.

The author studied the social causes that might influence the onset of dystrophy in two groups of families. A comparison of these causes revealed several social factors that limit the pediatrician's success especially in groups with a low standard of living.

FROM THE AUTHOR'S SUMMARY.

Prematurity and Congenital Deformities

CONGENITAL ANOMALIES. J. WARKANY, Pediatrics **7**:607 (May) 1951.

The author recalls the period when the prevailing belief was that all congenital anomalies are genetically determined. The hypothesis that environmental factors acting after conception can lead to developmental malformations lacked—in mammals and man—experimental verification. The discovery of a method whereby dietary restriction of specific essential nutriments can be used in the rat to produce anomalous development made possible the carrying out of large numbers of experiments and brought the verification. Additional implications of the experimental results are also discussed, including the importance of the specific nature of the dietary restrictions in bringing insight into the chemistry of development. Knowledge is accumulating to temper the pediatrician's eugenic advice when he is interrogated about the advisability of parenthood.

FROM THE AUTHOR'S SUMMARY.

GRIPPAL INFECTIONS DURING PREGNANCY AND EFFECTS ON OFFSPRING. M. SCHACHTER, Ann. pædiat. **175**:389 (Nov.) 1950.

Schachter reports the cases of three children whose mothers had an influenzal infection during pregnancy. In two of these cases, in which the infection occurred early in pregnancy, the children had somatic malformations with or without corresponding mental damage, but in both other etiological factors may have come into play (consanguinity and alcoholism of the parents). In the third case, in which the infection occurred toward the end of pregnancy, the child was normal. His character and educational difficulties seem to be due to psychological trauma from his family surroundings.

FROM THE AUTHOR'S SUMMARY.

THREE CASES OF DOLICHOSTENOMELIA—MARFAN'S SYNDROME. L. LANDUCCI, Lattante **22**:65 (Feb.) 1951.

Each of three cases presented some of the multiple characteristics found in arachnodactyly (dolichostenomelia, or Marfan's syndrome): abnormally long and thin phalanges, dislocation of the lens, congenital malformations of the heart, oxycephaly, bradycephaly, hydrocephalus, dislocation of the joints of the hip and clavicle, and other skeletal deformities. Two of the children, a brother and sister, also were markedly deficient mentally and displayed the Ehlers-Danlos syndrome—cutis laxa, vascular fragility, and many contusions and hematomas.

HIGGINS, Boston.

PROGNOSIS AS TO MENTALITY OF PREMATURE INFANTS, WITH A REPORT OF NEUROMENTAL DEVELOPMENT OF AN 860-GM. PREMATURE INFANT. M. SCHACHTER, Minerva pediat. **2**:355 (July) 1950.

A 14-year-old girl, who had been a 6½ month, 860 gm., premature infant, showed left hemiatrophy and had an intelligence quotient of 42; her head had the circumference equal to that of a 5-year-old child, and her height and weight were slightly subnormal for her age; she had normal sexual development.

Binet-Simon tests were given to 183 children who had been premature infants. Of the group, 41% were of normal mentality, 28% were of borderline mentality, and 31% were definitely feeble-minded.

HIGGINS, Boston.

MORTALITY OF PREMATURE INFANTS AT THE HOSPITAL INFANTIL OF MEXICO. CARLOS BAEZ DIAZ, Bol. méd. Hosp. inf., México **70**:657 (Oct.) 1950.

In the present statistical study the author analyzes the mortality of 911 premature infants who were admitted to the Hospital Infantil of Mexico from June, 1943, to July, 1949. For the study the author selected only those infants who were under 10 days of age at the time of their admission. Other factors were also taken into account: weight, sex, functional capacity, intercurrent diseases, and, more especially, diarrheas and bronchopneumonias, malformations and congenital diseases, and probable causes of death.

The results showed that in the premature service the mortality for the six years studied was 90.8% for those with a weight under 1,000 gm.; 65% for those from 1,001 to 1,500 gm.; 49.1% for those from 1,501 to 2,000 gm., and 44.7% for those from 2,001 to 2,500 gm.

It may be seen that the mortality of the 1,501 to 2,500 gm. group is very high; on the other hand, the mortality of the lighter weight groups is much the same as that prevailing at similar institutions. With the exception of those patients with weights between 1,501 to 2,000 gm., the trend of the mortality for the six years studied is definitively descending. The morbidity and mortality from diarrheas and bronchopneumonias were also high.

In order to establish a prognosis, it is necessary to study the functional capacity of the premature infant at admission. The high mortality of the heavier premature infants is mainly due to the fact that these infants are brought into the hospital late and in the worst of conditions, after the parents, through ignorance or carelessness, have tried to care for them at home without having the necessary training.

Other factors related to the high mortality are also analyzed, and the author concludes with several suggestions for diminishing the premature mortality in the Hospital Infantil of Mexico.

FROM THE AUTHOR'S SUMMARY.

Newborn

ORAL PENICILLIN IN THE NEWBORN. B. LEVIN and CATHERINE A. NEILL, Arch. Dis. Childhood **24**:171 (Sept.) 1949.

The blood levels following (*a*) a high dose of 20,000 units of penicillin every three or four hours and (*b*) a lower dose of 5,000 units a pound (453 gm.) in 24 hours have been ascertained in a group of infants under one month of age. It is shown that while the lower dose frequently gives an adequate level, the higher dose is preferable, since an adequate level is reached in almost all cases. The authors suggest a routine dose of 20,000 units a pound in 24 hours.

The factors influencing the higher blood levels in infants as against older children are discussed. It is shown that higher blood levels are associated with decreased fluid intake and that the younger the infant, the higher, in general, the blood level. No completely acceptable explanation of the difference has been found, but it is thought that either better absorption from the small intestine or less destruction in the colon may be a much greater factor than has been supposed. In minor skin lesions in infants penicillin administered orally appears slightly superior to sulfathiazole paste applied locally.

KELLY, Milwaukee.

UREA CLEARANCE IN THE IMMEDIATE POST-NATAL PERIOD. JOHN THOMSON, Arch. Dis. Childhood **24**:180 (Sept.) 1949.

The urea-clearing power of the kidney in the immediate postnatal period has been investigated in three groups of infants. Group 1 was a normal group comprising nine boys. Group 2 consisted of 13 boys, and group 3 consisted of 16 girls. At the commencement of the observation period 3 gm. of urea in 30 ml. of water was given by gavage to groups 2 and 3. The urea clearances in group 1 are considered to be normal clearances, those from groups 2 and 3 to be maximum clearances. Comparison of urea clearance between groups 1, 2, and 3 suggests that normally at urine minute volumes of 0.05 ml. or less urea clearance is maximum, but at greater urine minute volumes the urea clearance is normally less than maximum. Comparison of urea clearance in groups 1, 2, and 3 with urea clearance in infants over a week old shows that normally less urea is cleared in the immediate postnatal period. Comparison of maximum

urea clearance in the immediate postnatal period with the urea clearance of a standard adult having a surface area of 1.73 square meters and a weight of 70 kg. shows that on either basis of comparison urea clearance in the immediate postnatal period is less efficient.

KELLY, Milwaukee.

HEPATIC CIRRHOSIS FOLLOWING NEONATAL JAUNDICE. E. HINDEN, Proc. Roy. Soc. Med. **42**:560 (July) 1949.

A patient, the sixth child of healthy parents, was born with extreme jaundice. Both parents were Rh positive, and the mother's Wassermann reaction was negative. Jaundice had persisted for four months, when the liver was noticed to be enlarged; the spleen was not palpable. At one year of age both spleen and liver were enlarged and hard, and the child showed marked fat intolerance and failure to thrive. At 3 years of age she was admitted to the hospital suffering from a minor respiratory infection. Her liver and spleen were still enlarged and hard. The following day she sustained a severe hematemesis, from which she did not recover, in spite of prompt transfusion.

In the postmortem examination the liver was found to be grossly distorted and covered with a thick hyperplastic layer as in perihepatitis. It showed marked degeneration. Histologic study disclosed coarse Laennec's cirrhosis of the liver and coarse fibrosis of the spleen. Bleeding came from a massive esophageal varix.

WILLIAMSON, New Orleans.

THE IMPORTANCE OF NEONATAL MORTALITY. M. MOINE, and C. MOINE, Presse méd. **57**:103 (Jan. 29) 1949.

Parallel study of the figures for infant mortality in France and in the United States from 1930 to 1947 reveals a sharp upward curve in the French figures after 1940, while the curve for the United States continues downward. This can be explained by the precarious state of existence of the French infant under conditions of war and occupation.

On a breakdown of these figures, it is shown that the number of stillbirths is approximately equal in the two countries. This classification is not comparable between France and the United States, because of the difference in the legal interpretation of "stillborn." If the deaths within five days of birth are added to the stillbirths, the French totals are actually less than those for the United States. This, to the authors, presents proof that the increased mortality rate for French infants over 5 days of age is due to correctible nutritional and hygienic factors.

DAFFINEE, Melrose, Mass.

PROGNOSIS IN CASES OF PATHOLOGICAL PREGNANCY OR OBSTETRICAL TRAUMA. M. SCHACHTER, Lattante **20**:329 (June) 1949.

A statistical study was made of the physical and mental status of 62 children whose mothers had had either infection or toxemia during the pregnancy and of 353 children for which the delivery was instrumental or followed by asphyxia.

The percentages of children socially normal or capable of rehabilitation were about equal in the two groups. Speech was more frequently affected in the cases in which there had been obstetrical trauma, but the incidence of epilepsy was the same in the two groups.

HIGGINS, Boston.

SEVERE HEMOLYTIC DISEASE IN A FIRST-BORN CHILD OF AN RH-NEGATIVE MOTHER WHO HAD RECEIVED PREVIOUSLY INTRAMUSCULAR INJECTIONS OF RH-POSITIVE BLOOD. G. SANSONE, Lattante **20**:425 (July) 1949.

A 5-year-old, mentally deficient boy had had severe icterus neonatorum. The boy's mother, one and one-half years before the birth of this, her first, child, had twice received intramuscular injections of her mother's blood. The child and the grandmother were found to be Rh positive and the mother Rh negative. Thus a probable explanation of the jaundice and the mental deficiency of the boy was established five years later.

HIGGINS, Boston.

SEVEN ADDITIONAL CASES OF HEMOLYTIC DISEASE OF THE NEWBORN. A. PIGNERO and ANNA STEFANINI, Lattante **21**:663 (Oct.) 1950.

This article supplements a series of 20 case reports of hemorrhagic disease of the newborn in Leghorn, Italy. Of the live births in the maternity wards of the Leghorn Hospital during the past two years, 0.65% were of infants with hemorrhagic disease. Of the seven patients discussed in this paper, three died. Of the surviving four, all appeared to be normal mentally as well as physically when seen at the age of 9 months. It is important to begin transfusion therapy immediately after the diagnosis is made.

HIGGINS, Boston.

INTESTINAL OCCLUSION IN THE NEWBORN. C. MARINI, Lattante **21**:687 (Nov.) 1950.

Two cases of intestinal obstruction in newborn infants are reported. The cause in one case was a volvulus in the sigmoid; the condition was corrected at operation, the infant recovering after a very stormy course. The other infant had an atresia of the ileum; death occurred shortly after operation. The embryology of congenital intestinal occlusion is discussed. Early operative intervention and the plentiful use of antibiotics are advised.

HIGGINS, Boston.

GASTRIC ULCERS IN THE NEWBORN. P. G. BIANCHI and S. ZANARDI, Minerva pediat. **1**:264 (July) 1949.

Ulcers in the stomachs of five newborn infants were found at autopsy. In none of them had a clinical diagnosis of gastric ulcer been made. Three of the infants were premature, and the deaths had occurred between the second and the eighth day of life. The primary causes of death had been congenital syphilis (one), intracranial hemorrhages (two), hydrocephalus (one), and congenital heart lesion (one). The conclusions are drawn that the ulcers would have healed had the infants survived and that the ulcers had a neurotrophic causation, a cerebral alteration unbalancing the normal vegetative growth.

HIGGINS, Boston.

ANATOMICAL AND CLINICAL STUDY OF THE LIVER DAMAGE IN THE NEWBORN INFANT OF A MOTHER SUFFERING FROM EPIDEMIC HEPATITIS. F. TOSCANO and G. ROSSI, Pediatria **58**:209 (March) 1950.

An asthmatic mother had had an infectious jaundice for five weeks before the birth of a premature infant. The infant was jaundiced at birth and died on the sixth day. A postmortem examination was performed. The conclusion was reached that the infant's death was due to toxemia rather than to the transmission of the infection from the mother.

HIGGINS, Boston.

FETAL ERYTHROBLASTOSIS AFTER RH SENSITIZATION BY VERY SMALL AMOUNTS OF BLOOD. GUNTHER STARK, Deutsche med. Wchnschr. **76**:517 (April 13) 1951.

The newborn infant of a primipara became icteric three hours after birth. The illness is designated as "severe icterus gravis." The father was type O, Rh positive and the mother type O, Rh negative; the infant was type O, Rh positive. The mother's serum at the time of the infant's birth had a 1:256 titer of blocking antibodies, which were also present in the infant's blood, and presented low values for hemoglobin and erythrocytes; no further data are given. The infant received two transfusions and recovered without being severely ill. The sensitization of the mother was referred to a prophylactic injection against poliomyelitis of 15 ml. of Rh-positive blood.

AMBERG, Rochester, Minn.

THE PROBLEM OF RH-HAPTENE PROPHYLAXIS. R. HOLLANDER, Med. Klin. **46**:441 (April 6) 1951.

A previous infant, live-born, of an expectant Rh-negative mother had died with erythroblastosis. Another baby had been kept alive with difficulty. The mother's blood gave a positive test for univalent, a negative one for bivalent, antibodies. Eight months from the beginning of

the present pregnancy treatment with haptene was started. A normal, Rh-positive girl was born. The author realizes that no valid conclusion with regard to the value of the haptene treatment can be drawn from one observation.

AMBERG, Rochester, Minn.

ERYTHROBLASTOSIS IN CLINICAL PRACTICE. K. POLÁČEK and K. KUBÁT, Pediat. listy **5**:22, 1950.

Of 2,220 pregnant women who were examined at the three obstetrical clinics in Prague, 427 (19.2%) were Rh negative. Of 327 Rh-negative women with incompatible mates, 10% were appreciably and 20% slightly isoimmunized. One-third of the appreciably isoimmunized (sensitized) women gave birth to children with fetal erythroblastosis. Four of these had fetal hydrops; five had icterus gravis, and one had neonatal anemia.

The total frequency of manifest fetal erythroblastosis was one in 220 births. Transfusion of unknown-Rh blood was responsible for nearly 50% of the cases. Not counting the cases which were caused by blood transfusion, fetal erythroblastosis occurred in about 1% of cases of Rh-negative women. It never occurred in the first two pregnancies.

In the severe cases early exchange transfusion was the only successful treatment, and this only if it was performed before the clinical picture had come to its full development; therefore, correct estimation of the prognosis is of decisive value for successful treatment. Serology, clinical picture, and history are discussed and analyzed in detail from the point of view of their value for the indication to treatment. The mortality for all cases of fetal erythroblastosis was 50%, that for icterus gravis 20%. Desensitization of the mother will be the final therapeutic solution.

FROM THE AUTHORS' SUMMARY.

SEVERE ANEMIA IN A NEWBORN INFANT. H. UHRBRANDH, A. SOEBORG-OHLSEN, and E. FREIESLEBEN, Nord. med. **42**:1777 (Nov. 11) 1949.

A full-term boy, third child of the family, with two sisters healthy, showed jaundice on the first day which increased markedly on the third and fourth day of life. One week later a severe anemia was found, with hemoglobin content 20%, red blood cells 520,000, leucocytes 33,440 per 3 cu. mm., icteric index 1.9, and reticulocytes 2.4%. In the bone marrow there were signs of marked regeneration with a great number of immature cells of the white and the red system. Erythrocytes varied between 5 to 10 μ. Mother and child were Rh positive with identical A-B-O-genotypes. The child belonged to group O. Intoxication as well as syphilis and other infections were excluded. Treatment with blood transfusions was effective. Liver therapy was without effect. The child recovered in two months.

WALLGREN, Stockholm, Sweden.

RH IMMUNIZATION OF RH-POSITIVE MOTHER. BIRGER BROMAN, Nord. med. **43**:218 (Feb. 3) 1950.

Broman reports on 250 Rh-immunized mothers, examined during the past two years. Five of them, 2%, were Rh positive. It is pointed out that in cases of suspected erythroblastosis fetalis or hemolytic blood transfusion accidents in which the mother or the recipient is found to be Rh positive, this knowledge alone does not suffice to rule out the possibility of an Rh immunization. In such cases a more detailed Rh investigation should be made. A table with an English text shows the results of the investigation. All five of the children of Rh-positive mothers had erythroblastosis fetalis and died during the newborn period.

WALLGREN, Stockholm, Sweden.

SCLEREMA NEONATORUM. OLAV LUND, Nord. med. **43**:467 (March 17) 1950.

The infant reported had a birth weight of 4,200 gm., had been born by forceps extraction. Bleeding from the umbilicus produced a severe anemia that was treated with transfusions and administration of saline solutions subcutaneously. Thirty-six hours after birth sclerema of rather general localization developed. On the seventh day amelioration started, and the child was discharged as recovered. Treatment consisted only in blood transfusions.

WALLGREN, Stockholm, Sweden.

SPONTANEOUS PERFORATION OF THE COLON IN NEWBORN INFANTS. IVAR QVIGSTAD, Nord. med. **43**:504 (March 24) 1950.

A newborn boy displayed signs of intestinal stenosis on the fourth day of life and died two days later from ileus. At the postmortem examination a muscular defect at the site of the perforation in the transverse colon was demonstrated. The author is of the opinion that this defect plus a slight increase of the intraintestinal pressure may be the cause of the perforation.

WALLGREN, Stockholm, Sweden.

ERYTHROBLASTOSIS FETALIS AND PRENATAL CARE. G. J. KLOOSTERMAN, Maandschr. Kindergeneesk. **18**:146, 1950.

Erythroblastosis fetalis is a highly polymorphous syndrome usually encountered only in children of parents with Rh antagonism. This Rh antagonism, however, is to be regarded not as the cause of the syndrome as such but rather as the necessary condition for producing the syndrome. If this condition is fulfilled (Rh antagonism between mother and child), erythroblastosis develops in a very low percentage of cases (probably 5%).

The development of this sensitization is due to two serological factors: (1) an abnormally high tendency of some mothers to react rapidly to small quantities of Rh antigens by the formation of antibodies; (2) an abnormally strong antigen power of the Rh factor itself in some families. Further, at least one anatomical factor is present: an abnormal permeability of the placenta by Rh antigens.

When serological factors play the chief role, the so-called classic syndrome of erythroblastosis fetalis will develop most frequently, and treatment of the pregnant woman with a salt-free diet will have practically no beneficial effect. But if degenerative anomalies in the placenta are foremost factors in the pathogenesis, fewer characteristic syndromes will be encountered in the children, and a salt-free diet will often have good results.

Van Bolhuis is of the opinion that the placenta plays an important part, in that in comparatively few cases is the Rh antigen present in this organ. According to him, the mother will be sensitized by placental Rh antigens; this would explain why sensitization occurs in only a few cases of Rh antagonism. The observations of van Bolhuis are highly interesting, but it appears that he has indicated the consequence rather than the result. For if the placenta, which varies in every pregnancy, were to contain Rh antigen in only a small number of cases, it is not conceivable that some mothers repeatedly have placentas containing Rh antigen, and others, hardly ever.

FROM THE AUTHOR'S SUMMARY.

Acute Contagious Diseases

TREATMENT OF POLIOMYELITIS INVOLVING THE RESPIRATORY SYSTEM. HAROLD E. WEST and ALBERT G. BOWER, Am. J. M. Sc. **217**:252 (March) 1949.

The management of patients suffering from poliomyelitis with respiratory involvement requiring the use of a respirator has been presented. The indications for tracheotomy and the type of tracheotomy preferred have been described. The value of performing an early tracheotomy has been stressed.

Prevention of mechanical difficulties which arise from time to time in the management of patients suffering from acute poliomyelitis and in a respirator cannot be overemphasized. Adequate nursing care is essential. In the authors' opinion, the treatment described definitely has reduced mortality at least 50% for patients with acute bulbar poliomyelitis in the respirator who have had a tracheotomy performed.

HENSKE, Omaha.

THE PNEUMONIA OF MEASLES. LOUIS WEINSTEIN and WILLIAM FRANKLIN, Am. J. M. Sc. **217**:314 (March) 1949.

Pneumonia was found in 25% of 163 cases of measles. Pulmonary complications appeared to be commoner in children under the age of 5 years than in older children. Of the patients studied, in 50% the bronchopneumonia developed in the early stages of the eruptive phase of rubeola.

The definitive diagnosis of serious pulmonary involvement in measles was difficult because of the frequency with which the uncomplicated exanthem is accompanied with physical and roentgenographic abnormalities in the lungs. The application of certain clinical and laboratory criteria was of help in establishing the diagnosis of pneumonia. Most of the serious bronchopneumonias which occurred in the course of rubeola appeared to be due to Gram-positive bacteria. Penicillin appears to be the agent of choice in the treatment of pneumonia in measles; in a group of 40 patients treated with this drug, there was not a single fatality.

HENSKE, Omaha.

THE VALUE OF THE LABORATORY IN THE DIAGNOSIS OF POLIOMYELITIS. M. J. FOX and HOBART E. WALLACE, Am. J. M. Sc. **217**:401 (April) 1949.

An outbreak of a disease resembling poliomyelitis occurred in the Milwaukee area during the summer of 1947. This disease varied in certain unusual respects from that of the "typical" poliomyelitis outbreaks seen in previous years and was strikingly different from that of the outbreak seen the year before. Serum from afflicted patients of the 1947 outbreak did not reveal the presence of several types of encephalitis in this group. However, no studies could be made of the stools of these patients for the presence of the poliomyelitis virus.

The need for facilities to study patients for the presence of poliomyelitis and other viruses exists in most fever hospitals throughout the country. South View Hospital in Milwaukee is no exception to this need. The authors believe that when the viral laboratory becomes an active part of most fever hospitals, definite progress will be made in the study of the nature of poliomyelitis and the answers to its protean nature.

HENSKE, Omaha.

POLIOMYELITIS: IV. A STUDY OF THE MIDBRAIN. H. A. MATZKE and A. B. BAKER, A. M. A. Arch. Neurol. & Psychiat. **65**:1 (Jan.) 1951.

Pathologic studies show that the midbrain is never involved as severely as the lower region of the brain stem, although it is frequently included in the pathologic processes of poliomyelitis. Most severely affected portions are the oculomotor nuclei, substantia nigra, and tegmental nuclei. Clinically, patients show little evidence of midbrain involvement, except for the oculomotor centers, where the clinical findings correlate fairly well with the degree of involvement of the nuclei.

MCGUIGAN, Evanston, Ill.

THE CONCENTRATION OF MUMPS VIRUS. GEORGE F. FORSTER and ESTHER CARSON, J. Infect. Dis. **85**:62 (July-Aug.) 1949.

The alcohol precipitation method which Cox and his associates have found highly satisfactory for concentration of influenza virus is equally useful for concentrating mumps virus grown in the allantoic sac of the chick embryo.

Mumps virus will agglutinate the red blood cells of chickens, guinea pigs, human beings, and sheep, the latter with less regularity. Adsorption of the virus on the red blood cells of each of these species will occur, but consistently it does so in greater degree when the cells of sheep are used.

Enhanced adsorption of mumps virus occurs when denser suspensions of the red blood cells of any of these species are used, but the greater effectiveness of sheep erythrocytes as an adsorption vehicle is apparent at all densities tested (up to 30% suspensions).

TOOMEY, Cleveland.

THE PROGNOSIS OF FACIAL NERVE PARALYSIS IN POLIOMYELITIS. HENRY RASCOFF, J. Pediat. **35**:567 (Nov.) 1949.

Rascoff observed 23 children with facial paralysis due to poliomyelitis. Nineteen of these children had no other nerve involvement. Twelve children recovered completely, 10 children showed slight permanent paralysis, and 1 child retained a marked permanent paralysis. Treatment did not seem to alter the course of the disease.

MACDONALD, Pittsburgh.

IMMUNE RESPONSES AND REACTIONS TO DIPHTHERIA AND TETANUS TOXOIDS, WITH PERTUSSIS VACCCINE, ALUMINUM PHOSPHATE PRECIPITATED. JAMES A. MCCOMB and MARION Z. TRAFTON, New England J. Med. **243**:442 (Sept. 21) 1950.

Diphtheria and tetanus toxoid with pertussis vaccine, precipitated by aluminum phosphate, was injected intramuscularly into an unspecified number of children for a total of 765 injections. None of the children had had prior tetanus immunization, and the status of the existing diphtheria and pertussis immunization was undetermined.

Three doses of 0.5 cc. were given four weeks apart, and 134 booster doses were also given, and local or general reactions were not severe. One month after the last dose tetanus antitoxin levels were determined in 71 cases and found to be 100% adequate in all.

The status of this product in regard to diphtheria and pertussis immunization cannot be accurately evaluated because of lack of preinjection blood titers. WHEELOCK, Denver.

EPIDEMIC POLIOMYELITIS. HARRY M. WEAVER, New England J. Med. **243**:1019 (Dec. 28) 1950.

For 12 years adequate funds for an intensive research effort against poliomyelitis have been available. The results of this effort and the possibilities for the future are concisely delineated in this article.

Control of this disease involves the discovery of agents or procedures which can interrupt the chain of events which characterizes the progression of the virus in a human and from person to person. Therapy in poliomyelitis is best used to describe treatment administered to a patient after he has acquired the signs and symptoms of the clinical disease, rather than after an infection with the virus, which is subclinical in many instances.

Nonspecific therapy has as its objectives the prevention or arrest of the progression of paralysis, the reduction in crippling, and the saving of lives. The true effect of modern, expensive, nonspecific therapy is difficult to assess in view of the vagaries of the illness. The author believes that bed rest in the preparalytic stage reduces subsequent paralytic tendencies, that lives are saved in patients whose vital nerve cell damage is severe but reversible, that nonspecific stress, such as tonsillectomy, exhaustion, and pregnancy, affects adversely the defense barriers against the severer forms of the clinical disease, and that orthopedic science has reduced crippling deformity.

Specific therapy for poliomyelitis virus victims, in the form of chemical or biologic agents, still does not exist, nor does vaccination or serotherapy offer any aid if given after nerve cell invasion.

The best protection against paralytic poliomyelitis is to be born of a poliomyelitis-resistant mother and to be exposed to the virus frequently from early infancy through maturity. Today, however, a considerable number of humans are born without passive protection against the various viruses of poliomyelitis. In addition, many persons do not become infected frequently with the virus as they grow from infancy to adulthood. Therefore, vaccination, seroprophylaxis, and chemoprophylaxis should theoretically be effective in preventing the paralytic consequences of virus invasion. A practical vaccine given by an effective route at the most opportune time is not yet available.

Also, it is as yet unwise to carry out large-scale human experiments with immune serum in the hope of preventing paralytic poliomyelitis. The reasons for this are given.

Chemical agents which affect the virus adversely or render the nerve cell inhospitable for virus propagation are also not practical, but there is ample provocative evidence in all these fields of endeavor to direct energy and effort forward. WHEELOCK, Denver.

URINARY DIASTASE IN MUMPS. MARTIN M. NOTHMAN, New England J. Med. **244**:13 (Jan. 4) 1951.

Serum diastase levels are increased during the course of mumps. Urinary excretion of this enzyme is also increased, and the author utilized the determination of the amount of this material in the urine as a confirmatory diagnostic test for mumps in 27 children and three adults

who had this disease. The urinary diastase level was increased in every case over the 80 to 350 units taken as a normal figure.

Since patients with puzzling, but suggestive, facial swellings not of mumps origin do not have elevated urinary diastase levels, this test is useful in differential diagnosis. Mumps which may involve only glands other than the parotids generally show diastase elevation in the urine even if the parotids are not affected. The applications of this valuable test are self-evident.

WHEELOCK, Denver.

PRESENT-DAY CONCEPTS OF IMMUNIZATIONS OF INFANTS. E. ALBERT MOODY, Northwest Med. **50**:30 (Jan.) 1951.

There has been a recent trend to immunize infants at an earlier age than has been the custom in the past. Early immunizations of infants has been chiefly concerned with protection against pertussis. With the use of combined immunization products, however, the feasibility of early combined immunization is presented.

The main arguments against early immunization, as presented by McKhann, Sauer, and others, are contrasted with the statements of Sako, Halpern and Halpern, Miller, and others, whose results tended to show adequate antibody response from immunizations begun at 2 to 4 weeks of age.

The author concludes that immunizations should be started at 4 to 6 weeks of age. This will effect at least a partial protection against pertussis at an age when its mortality is the highest.

DOCTER, Seattle.

IMMUNIZATION AGAINST PERTUSSIS DURING THE FIRST FOUR MONTHS OF LIFE. JOHN J. MILLER JR., HAROLD K. FABER, MARY LOUISE RYAN, ROSALIE SILVERBERG, and EDITH LEW, Pediatrics **4**:468 (Oct.) 1949.

Agglutinative reactions with Hemophilus pertussis were determined on 108 pairs of maternal and cord blood serums. A correspondence in titer within the range of experimental error was demonstrated in 77% of the pairs. Fifty per cent of the maternal serums contained demonstrable agglutinins. Transplacental transmission of antibody was demonstrated for 63% of the 54 seropositive mothers.

Saline-suspended H. pertussis vaccine was administered to infants on the fifth day of life and at 1 and 2 months of age. With total doses of 50,000,000,000 H. pertussis, only 15% of 41 infants produced agglutinins in a titer of 1:320 or higher—the level which in older children has been found consonant with clinical immunity. When the total dose in a second group of infants was increased to 100,000,000,000 H. pertussis, the above titer was demonstrated in 25% of 145 infants.

The serologic response of infants whose cord blood had contained no agglutinins was not superior to that of infants with agglutinins. Thus, no depression of the immune response by transplacentally acquired antibody was demonstrable.

In a third group of 134 slightly older infants saline-suspended H. pertussis vaccine was administered in a total of 80,000,000,000 cells divided into three monthly injections. The first injection was given at 4 to 8 weeks of age. Forty-eight per cent of these infants had agglutinins in a titer of 1:320 or higher. However, three months later only 36% were carrying this high titer. General febrile reactions were not uncommon, and one proved case of mild pertussis occurred in this group.

In a fourth group of 151 infants alum-precipitated H. pertussis vaccine was injected in a total dose of 40,000,000,000 cells divided into three injections at monthly intervals. The first injection was given at 4 to 8 weeks of age. Only two febrile reactions, one associated with a local reaction which did not break down, occurred. In 62% of 115 infants whose serums were tested four to eight weeks later H. pertussis agglutinins in a titer of 1:320 or higher had developed. Twelve months later 60% still carried these high titers. This satisfactory response at this age with this product is confirmatory of the studies of Sako, Treuting, Witt, and Nichamin. It adds support to their thesis that active immunization with alum-precipitated vaccine can be accomplished before the sixth month of life.

A schedule for immunizations during the first year of life, embodying H. pertussis immunization beginning at 4 to 8 weeks of age, is described.

FROM THE AUTHORS' SUMMARY.

HUMORAL ANTIBODY FORMATION IN INFANTS AGED ONE TO THREE MONTHS INJECTED WITH A TRIPLE (DIPHTHERIA-TETANUS-PERTUSSIS) ALUM-PRECIPITATED ANTIGEN. WILLIAM L. BRADFORD, ELIZABETH DAY, and FREDERICK MARTIN, Pediatrics **4**:711 (Dec.) 1949.

Immunization of infants aged 1 to 3 months with an alum-precipitated antigen containing diphtheria and tetanus toxoids and Hemophilus pertussis organisms resulted in satisfactory humoral antibody levels against diphtheria and tetanus. Ninety-seven per cent of the subjects tested revealed more than the generally accepted level of protection against diphtheria; and 94% showed a similar result against tetanus.

In regard to pertussis, only a few of the immunized infants had agglutinative titers of 1:320 or higher. However, analysis of the titers in terms of the expected number of cases of pertussis, if the infants were subjected to family exposure, indicates that probably 75% of the infants were protected.

When tested six months after the completion of the original series of injections, each of 29 infants gave positive skin reactions to the injection of agglutinogen.

FROM THE AUTHORS' SUMMARY.

USE OF AUREOMYCIN AND PENICILLIN IN THE TREATMENT OF RUBEOLA. S. KARELITZ, H. KING, B. CURTIS, and M. WECHSEL, Pediatrics **7**:193 (Feb.) 1951.

Neither aureomycin nor penicillin given to children with pre-eruptive rubeola or begun on the first day of rash seems to have any definite therapeutic effect on the course of the primary disease. The temperature dropped earlier in the patients treated with aureomycin or penicillin than in the untreated control group. Aureomycin and penicillin were effective against otitis media and pneumonia present on admission and on the complications which developed during the disease. Aureomycin and penicillin are useful in the prevention and cure of secondary infection in rubeola.

FROM THE AUTHORS' SUMMARY.

SOME EXPERIENCES WITH THE AFTER CARE OF POLIOMYELITIS. F. H. H. NEWBURN, Canad. M. A. J. **61**:286 (Sept.) 1949.

A brief discussion of poliomyelitis and its varying manifestations is followed by a résumé of treatment used by the author. In the acute stage rest and heat are advised, with attention to the prevention of deformities. In the convalescent state physiotherapy, with surgical treatment when needed after two years, is recommended.

McGUIGAN, Evanston, Ill.

AMAUROSIS IN WHOOPING COUGH. N. W. WOYWITKA and J. V. RICHES, Canad. M. A. J. **63**:272 (Sept.) 1950.

Two cases of amaurosis in sisters suffering from severe whooping cough are reported. Recovery was complete in five months. Toxis encephalitis is presumed to be the cause of the amaurosis.

McGUIGAN, Evanston, Ill.

AUREOMYCIN AND MUMPS. S. J. SHANE and G. W. SODERO, Canad. M. A. J. **63**:387 (Oct.) 1950.

In a patient under treatment with aureomycin mumps developed. Apparently aureomycin is of no value in the treatment of mumps.

McGUIGAN, Evanston, Ill.

ENCEPHALITIS AND MENINGOENCEPHALITIS IN MUMPS. D. GOTTI, Clin. pediat. **32**:489 (Sept.) 1950.

Ten cases of mumps meningoencephalitis were diagnosed in the Children's Clinic in Bologna over a period of seven years. In this same period, 3,306 cases of mumps and 128 cases of polio-

myelitis were reported in the Commune of Bologna. Mumps meningitis without accompanying parotitis may be diagnosed as poliomyelitis, if care is not taken. HIGGINS, Boston.

STREPTOMYCIN THERAPY BY INHALATION IN PERTUSSIS. P. L. BOSCO and G. CACI, Lattante **21**:648 (Oct.) 1950.

Fifty-six children with pertussis were given streptomycin by aerosol for periods of from 6 to 16 days. The daily dose for infants under one year was 0.4 gm., for children 1 to 3 years, 0.6 gm., and for children 3 to 6 years, 0.8 gm.; the daily dose was divided into four parts, inhalations being given every three hours during the daytime. This treatment produced a lessening of the frequency and severity of the coughing attacks, elimination of the vomiting, and prevention of secondary infections. Ten of the infants were tuberculous; the treatment also proved to be beneficial with regard to the tuberculous processes. HIGGINS, Boston.

STATISTICAL INVESTIGATION ON RELATION OF SUSCEPTIBILITY TO SCARLET FEVER AND BODY WEIGHT. FRITZ KUESTER and MARGRET VON BAUR, Arch. Kinderh. **137**:225 (Nov.) 1949.

Statistical analysis revealed that 893 boys, 1 to 11 years of age, who contracted scarlet fever had a body weight 3.7% higher than 1,039 boys of the same age group who remained free of scarlet fever. For 908 girls of the same age group who contracted scarlet fever the body weight was 3.0% higher than for 782 control girls who remained free of the infection. The difference between the body weight of the children who contracted scarlet fever and those who remained free of the disease is far above the statistical error. ARON, Chicago.

STATISTICAL INVESTIGATIONS ON RELATIONSHIP OF SUSCEPTIBILITY TO SCARLET FEVER AND BODY WEIGHT: II. CONDITION IN UNDERNUTRITION. FRITZ KUESTER and HEINZ GOEDECKE, Arch. Kinderh. **138**:27 (Dec.) 1949.

The analysis is based on a study of 1,207 children, 1 to 14 years of age, 573 boys and 634 girls, treated for scarlet fever during the years 1943 to 1948. In spite of the great reduction in the intake of animal protein during the war and the postwar period, the children who contracted scarlet fever were overweight as compared to control children who remained free of scarlet fever. The difference in body weight is statistically significant. The authors regard these findings as a proof that the susceptibility to scarlet fever depends primarily on the high water content of the tissues, regardless of how this is caused. ARON, Chicago.

HISTAMIN AND ACETYLCHOLIN CONTENT OF BLOOD AND SPINAL FLUID IN TOXIC CONDITIONS (DIPHTHERIA, SCARLET FEVER AND DYSENTERY). J. DIECKHOFF, Arch. Kinderh. **138**:49 (Dec.) 1949.

The blood of healthy children contains 20 to 30 γ of histamine per 1000 cc. In toxic types of diphtheria, scarlet fever, or dysentery, the histamine or histamine-like substances in the blood were found increased to 40 to 150 γ. The histamine level is usually higher the severer the toxic condition is. In the blood serum of toxic children no acetylcholine was found. In 14 cases of toxic diphtheria, scarlet fever or dysentery, acetylcholine was found in the spinal fluid in concentrations from $1:10^{6}$ to $1:10^{14}$. ARON, Chicago.

STREPTOMYCIN AND DIPHTHERIA. RUDOLPH, Monatsschr. Kinderh. **98**:74 (Feb.) 1950.

Guinea pigs given injections subcutaneously of a lethal concentration of diphtheria organisms were protected by simultaneous single intramuscular administration of streptomycin. A 12-hour-delay of streptomycin injection protected 5 of 25 animals. Antitoxin given alone 12 hours after infection with the diphtheria organisms protected only 1 of 25 animals, while combination of antitoxin and streptomycin given 12 hours after infection protected 12 of 25 guinea pigs.

HARTENSTEIN, Madison, Wis.

VACCINIA WITH OCULAR INVOLVEMENT: A CASE REPORT. CH'ANG-AN TENG, Chinese M. J. **669**:58 (Jan.-Feb.) 1951.

The patient was a 4-month-old girl. She had dry, hazy corneas, probably because of vitamin A deficiency. She was vaccinated against smallpox, and vaccinia developed involving the eyelids and cornea, with resultant scarring.

MACDONALD, Pittsburgh.

Acute Infectious Diseases

STREPTOMYCIN THERAPY FOR CHILDHOOD TULAREMIA. H. B. LEVY, C. H. WEBB, and J. D. WILKINSON, New Orleans M. & S. J. **103**:78 (Aug.) 1950.

Twenty-four patients with tularemia were cured by the administration of 125 mg. of streptomycin every three hours for five to six days. Response was rapid and often dramatic.

McGUIGAN, Evanston, Ill.

TULAREMIA AS PEDIATRIC PROBLEM. HAROLD B. LEVY, CLARENCE H. WEBB, and JACQUES D. WILKINSON, Pediatrics **6**:113 (July) 1950.

Childhood tularemia differs from the adult disease in the clinical form and source of infection. A study of 48 cases showed less than half (21 cases—44%) to be of the typical ulceroglandular type, with a new form, pharyngeal-tonsillar, designated because of 11 patients so classified. Typhoidal tularemia was seen in eight, glandular in six, and oculoglandular in two. Ingestion of infected material, and bite of infected ticks each accounted for one-third the total infections, the former being an outstanding source in the younger age groups. Involvement of siblings was a striking factor noted in the ingestion form. Absence of pathognomonic findings requires a high index of suspicion in order to obtain early diagnosis, which may later be confirmed by specific agglutination reaction.

Streptomycin is considered the present treatment of choice, excellent results having been obtained in 24 patients. Illustrative case reports demonstrate the rapid response to this antibiotic. With the lower dosage now recommended (0.5 gm. daily for six days), one may safely employ streptomycin as a therapeutic trial with minimal danger of toxic effects and often with definitive results in equivocal cases.

FROM THE AUTHORS' SUMMARY.

HIGH RENAL ECTOPIA AND CONGENITAL DIAPHRAGMATIC HERNIA. F. G. FLEISCHNER, S. A. ROBBINS, and M. ABRAMS, Radiology **55**:24 (July) 1950.

A herniated mass at the base of the right lung posteriorly, seen on chest roentgenograms, in a 65-year-old woman was identified by intravenous pyelography as an ectopic right kidney. It was located in the posterior and mesial portion of the diaphragm, a frequent location of hernias. The literature contains reports of 11 other such cases, but this seems to be the first instance in which the diagnosis was made during life. There were no clinical symptoms or signs referable to the anomaly.

ANSPACH, Chicago.

EFFICACY OF INTRAVENOUS SPECIFIC VACCINE THERAPY AND OF STREPTOMYCIN-SULFADIAZINE MEDICATION IN BRUCELLOSIS. D. GOTTI, Clin. pediat. **32**:429 (Aug.) 1950.

Satisfactory therapeutic results were obtained in most cases of undulant fever either with streptomycin-sulfadiazine therapy or with specific vaccine injections. There were some patients in whom the febrile episodes returned; these patients usually responded to vaccine therapy.

HIGGINS, Boston.

EFFECT OF VITAMINS ON AGGLUTINATION TITER IN BLOOD OF PATIENTS RECEIVING TYPHOID VACCINE. G. CALZETTI, Clin. pediat. **32**:469 (Sept.) 1950.

The giving of a vitamin at the time that typhoid vaccine was injected resulted invariably in an increased antityphoid titer in the blood after three or four weeks; the increase was greater with the fat-soluble vitamins A and D_2 than with the B complex vitamin and vitamin C. The

titer also rose much more rapidly with all the vitamins (except C) than it did in the control cases. The local reaction to the vaccine was found to be less in the subjects receiving the vitamins.

HIGGINS, Boston.

TREATMENT OF AMEBIASIS AND LAMBLIASIS IN CHILDREN. F. LO PRESTI-SEMINERIO, Lattante **21**:566 (Sept.) 1950.

The symptoms of amebiasis and giardiasis may be mild, such as malnutrition in the chronic cases, to severe, such as dysentery, toxemia, anemia, and convulsions, in the acute cases. The course of treatment depends upon the severity of the case. If possible, diagnosis should be established before treatment is begun. While emetine is the drug of choice in the acute phase of the disease, its continued use is inadvisable. The sulfonamides, penicillin, and streptomycin are of value only in that they may change the fecal flora.

HIGGINS, Boston.

DIETARY TREATMENT OF DYSENTERY IN CHILDREN. G. BONELL, Lattante **21**:656 (Oct.) 1950.

The dietary regimen followed at the Heidelberg University Pediatric Clinic in cases of dysentery is outlined and suggested as applicable to cases in Italy. Castor oil is given before food is started; then tea, carob flour, honey, cocoa, grated raw carrots, cheese, skim milk, bread, ground meat, and buttermilk are added to the feeding one after the other.

HIGGINS, Boston.

IRON CONTENT OF THE BLOOD SERUM IN LEISHMANIASIS INTERNA. P. DE CAPRIO, Pediatria **58**:170 (March) 1950.

Of 18 children with kala-azar before antimony treatment was begun, the iron content of the blood serum was above normal in 7, normal in 3, and subnormal in 11. There was no proportional relation between these results and the hemoglobin content or reticulocyte count of the blood.

HIGGINS, Boston.

STATISTICAL AND CLINICAL STUDY OF 260 CASES OF RHEUMATIC HEART DISEASE IN CHILDREN. F. PECORELLA and A. CORSELLO, Pediatria **58**:498 (July) 1950.

Rheumatic heart disease was seen in 260 children over a period of 40 years at the children's clinic and hospital of the University of Palermo, Sicily. These patients constituted approximately 0.5% of the total patients; this percentage has been quite constant over the entire 40 years. The disease was commoner in the winter and the spring, and among children living along the seacoast. Of the valvular lesions, 97% were of the mitral valve. Of 29 patients with chorea, 21 showed heart lesions.

HIGGINS, Boston.

SOME RARE FINDINGS IN A CASE OF SHIGELLA DYSENTERY. P. DE CAPRIO, Pediatria **58**:583 (July) 1950.

Two unusual findings in a case of dysentery in an 8-year-old boy were a positive blood culture (Shigella dysenteriae) and the occurrence of a nephrotic picture, first manifested about two weeks after the onset of diarrhea and toxicity. The urinary and blood findings of the kidney disorder persisted for about one month.

HIGGINS, Boston.

CASE OF SOLITARY CYST IN KIDNEY OF A SIX-YEAR-OLD BOY. A. RIGHINI, Riv. clin. pediat. **48**:663 (Oct.) 1950.

After some clinical considerations of the literature already existing on the subject, the author describes a case of solitary cyst in the kidney of a 6-year-old child (such anatomopathological forms being rare in pediatric surgery). He also describes the histological examination of the removed portion and the results of urography done before and after operation.

FROM THE AUTHOR'S SUMMARY.

CIRCULATORY SYSTEM IN CHILDHOOD BRUCELLOSIS. ANGEL S. SEGURA, Arch. argent. pediat. **32**:39 (July) 1949.

Seventy-seven cases of childhood brucellosis (in 36 males, 41 females, aged 1 to 13 yr.) are statistically surveyed. Only one patient had evidence of endocarditis, with cardiac enlargement. There was no electrocardiographic or roentgenographic evidence of cardiac involvement in the remainder. There was a tendency for reduced pulse pressure in approximately 65% of the patients. Tachycardia out of proportion to the degree of fever was present in 52%, and most of these had normal blood pressure. One patient had bradycardia. The author believes that specific involvement of the cardiovascular system in childhood brucellosis is rare, most of the changes being explainable on the basis of systemic disease or extrinsic factors. No statement is made regarding the number of cases in which the diagnosis was made by isolation of the organism on culture.

PANOS, Galveston, Texas.

NINE CASES OF TYPHOID TREATED INTRAVENOUSLY WITH AUREOMYCIN. ANDERS RODRIGUEZ MEZA and LUIS GOMEZ OROZCO, Bol. méd. Hosp. inf., México **7**:653 (Oct.) 1950.

The authors report on nine patients with typhoid who were treated with aureomycin intravenously. During treatment an improvement in the general symptomatology was noted. The final results were good in one case, doubtful in two; no results were obtained in the rest. There was one death. Phlebitis developed in two patients at the sites of injection of the drug.

FROM THE AUTHORS' SUMMARY.

CASE OF CONGENITAL MALARIA. LAZARO BENAVIDES V. and JUAN A. LASTRAS, Bol. méd. Hosp. inf., México **7**:697 (Oct.) 1950.

The authors report the case of a 38-day-old baby with malaria (Plasmodium falciparum) whose mother had malaria several days previous to and after delivery. He has been clinically ill since his third day of life, and the case is considered as probable congenital malaria, for both the patient and his mother have not been out of Mexico City, where P. falciparum and Anopheles do not exist.

FROM THE AUTHORS' SUMMARY.

PAROXYSMAL HEMOGLOBINURIA. GUSTAVO GORDILLO, Bol. méd. Hosp. inf., México **7**:707 (Oct.) 1950.

Gordillo reviews the medical literature on paroxysmal hemoglobinuria, giving the definition and the most important historical data. He points out modern etiopathogenic concepts and accepts paroxysmal hemoglobinuria as a manifestation of late syphilis, especially congenital. He believes that it is due to the presence of a hemolysin which is adsorbed at low temperature by the red blood cells, and which destroys them when the temperature is raised.

He describes the symptoms, stressing the frequent finding of associated Reynaud's syndrome. The main points needed to establish a diagnosis and the differential data with other hemoglobinuric diseases are mentioned.

The selective treatment is that of late syphilis: penicillin exclusively, or combined with arsenicals and bismuth salts; blood transfusions to correct the anemia; avoidance of exposure to cold, and the use of vasodilators to improve vascular disturbances. Mention is made of several patients successfully treated by other authors.

Presentation is made of two cases of late congenital syphilis with paroxysmal hemoglobinuria and Reynaud's syndrome. These are the first cases in patients seen at the Hospital Infantil. Laboratory and other tests confirmed the diagnosis. At present these patients are under treatment.

FROM THE AUTHOR'S SUMMARY.

TYPHOID AND CHLOROMYCETIN. RENE NAHMIAS ALBALA, Rev. chilena pediat. **20**:344 (Aug.) 1949.

In a case of typhoid with a bronchopneumonia complication in a 7-year-old child treatment was successful with chloramphenicol (chloromycetin®) and penicillin.

FROM THE AUTHOR'S SUMMARY.

MYELOGRAMS IN 40 CASES OF TYPHOID IN CHILDREN. RAUL EBERHARD E. and ENRIQUE MARMENTINI G., Rev. chilena pediat. **22**:47 (Feb.) 1951.

The authors study a series of myelograms made during the second, third, and fourth weeks of typhoid in 40 children between the ages of 4 and 12 years.

They point out the fact that as compared with the normal values, they have observed (*a*) an increase of the hemohystioblasts; (*b*) diminished number of bacilliforms, and (*c*) diminished number of orthochromatic erythroblasts.

They stress the different types of myelograms obtained as compared with the regular changes found in the blood.

FROM THE AUTHORS' SUMMARY.

AN EPIDEMIC OF TYPHOID WITH 156 CASES TREATED PREPONDERANTLY WITH CHLOROMYCETIN. FRANZ BECKERMANN and GERHARD OTTO, Deutsche med. Wchnschr. **76**:466 (April 6) 1951.

Of the 156 cases of typhoid, 114 concerned patients up to 16 years of age. The treatment with chloramphenicol (chloromycetin®) proved of great value. A safety medication, continued for two weeks after the last fever day, is recommended.

AMBERG, Rochester, Minn.

GONORRHEA IN CHILDHOOD. O. MAUDAUSOVÁ, Pediat. listy **5**:141, 1950.

The author gives a report of her experience in the treatment of gonorrhea in childhood. She considers it to be a nonvenereal infectious disease, because none of her nine patients acquired the disease by the genital route. It occurred in all age groups, but most frequently around the fifth year. An epidemic broke out among children living in a community (in a holiday camp). Diagnosis can be made only by microscopic examination of the Gram-stained smear and by culture. Complications were extremely rare (blennorrhea in two cases). The patients were first treated by sulfonamide tablets by mouth combined with sulfonamide tablets in the vagina; later, by the administration of 50,000 units of penicillin four times, given in a course of two days, combined with the introduction of 20,000 units of penicillin into the vagina in the form of vaginal suppositories. Microbiological examinations were made at least twice after treatment had been terminated. Relapse occurred in one patient. The prophylaxis does not differ from that in other infectious diseases.

To prevent epidemics all school girls of Prague suffering from vaginal discharge are subjected to a thorough clinical and microbiological examination at the children's gynecological department of the Polyclinic Prague before they are allowed to leave for holiday camps and convalescent homes.

FROM THE AUTHOR'S SUMMARY.

VAGINAL DISCHARGE APPEARING AT ABOUT AGE OF PUBERTY. M. OBRDOVÁ-DVOŘAČKOVA, Pediat. listy **5**:147, 1950.

Girls approaching the time of their first menstruation often suffer from a vaginal discharge. In most of these so-called pubertal discharges a great number of Döderlein's bacillus and epithelial and inflammatory cells are found microscopically. This discharge, like the others, is often the cause of inflammatory changes of the external genitalia, and in the future more attention should be paid to its origin and therapy.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF INFANTILE VAGINAL DISCHARGE. K. VESELY, Pediat. listy **5**:148, 1950.

The author reviews the principles of adequate treatment of infantile discharge based on a correct microbiological diagnosis and emphasizes the necessity of local treatment by the introduction of drugs, in the form of tablets and suppositories, into the vagina. Neonatal and pubertal discharge do not require treatment so long as they are provoked by Lactobacillus acidophilus alone, but as soon as pathogens are also present the author considers the discharge to be infectious and suggests local treatment with antibiotics in the quiescent period. Vaginal trichomoniasis appearing in the newborn and during puberty must be treated as in adults by the introduction into the vagina of trichomonicidal drugs. Mycotic infection (yeast-like fungi of

the genus Candida, C. albicans and others) should be treated with boric acid, the specific effect of which has been proved.

FROM THE AUTHOR'S SUMMARY.

ARECA NUT (BETEL NUT) AND OLEORESIN OF ASPIDIUM IN THE TREATMENT OF INTESTINAL TAENIASIS. HUEI-LAN CHUNG, TSUNG-CHANG HOU, TA-YOU HUANG, and HSIN-CHIH WENG, Chinese M. J. **69**:76 (Jan.-Feb.) 1951.

Areca nut is a nontoxic substance used for treating tapeworm. It is highly specific against Taenia solium and fairly potent against T. saginata. The decoction used is prepared as follows: 4 oz. (113 gm.) of dried areca nut in thin slices is gently boiled in 500 cc. of water for about two hours until a final volume of about 150 to 200 cc. is obtained. This is the total dose of the teniafuge. There is no preliminary preparation except to omit breakfast. The 150-cc. to 200-cc. decoction, prepared as above, is given at 7 a. m. Usually loose, watery stools with the entire worm and its head will be passed within two hours after the ingestion of the areca nut preparation. If there has been no bowel movement by 9 a. m., 50 cc. of 50% magnesium sulfate solution is given to hasten the passage of the worms. The authors treated 120 patients. The youngest was 3 years old, the eldest 64.

MACDONALD, Pittsburgh.

STEVENS-JOHNSON SYNDROME AND BOVINE CATARRHAL FEVER. GILLIS HERLITZ, Nord. med. **43**:659 (June 21) 1950.

Herlitz reports two cases of ectodermosis erosiva pluriorificialis (Stevens-Johnson syndrome), one in a 6-year-old and the other in a 4-year-old boy. These two cases were manifested at the same time and both after probable exposure to malignant catarrh of cattle. The author is of the opinion that something more than mere coincidence must be assumed. The incubation period of the acute malignant catarrhal fever is one to four months. It can never be transmitted with secretions from affected mucous membranes. The cause of the disease is thought to be a virus. Sheep act as passive carriers. From the sheep the virus is probably transmitted to the cow by some blood-sucking insect. The disease occurs in Sweden and is well known to veterinary surgeons. Experimental transmissions in the two reported cases of Stevens-Johnson syndrome could not be performed before the high-fever stage had passed. The loss of nails during the illness, which was observed in these cases, is discussed in relation to the loss of horns in malignant bovine catarrh.

WALLGREN, Stockholm, Sweden.

RHEUMATIC PERITONITIS SIMULATING ACUTE APPENDICITIS. JÖRGEN BOCK, Nord. med. **44**: 1285 (Aug. 11) 1950.

A 13-year-old boy was operated on for acute appendicitis. The peritoneum was found rather normal, the peritoneal fluid somewhat increased. Four days after operation polyarthritis occurred, with signs of heart involvement, increased conduction time (PQ interval 0.22 second), and systolic murmur of the heart. Sedimentation rate was 75 mm. The antistreptolysin titer was 450. He was discharged healthy three months later. Another case is reported of an 8-year-old boy who had an acute catarrhal infection and was operated on for acute appendicitis. The appendix was, however, normal and the peritoneum without significant abnormality. Nine days later he had pains in his left knee and foot joints. The antistreptolysin titer was 1,250. Auscultation was normal. The electrocardiogram was without significance. He was discharged two months later healthy. The author is of the opinion that the abdominal signs and symptoms in the two boys depended on peritonitis due to rheumatic infection.

WALLGREN, Stockholm, Sweden.

Chronic Infectious Diseases

CURRENT STATUS OF DRUG THERAPY IN TUBERCULOSIS. COMMITTEE ON MEDICAL RESEARCH AND THERAPY (AMERICAN TRUDEAN SOCIETY), Am. Rev. Tuberc. **61**:436 (March) 1950.

The introduction of several additional agents into the drug therapy of tuberculosis has increased the need for perspective in the consideration of the proper role of such drug therapy in the over-all treatment of tuberculosis. While these agents may now be employed with more

precision than previously, much remains to be determined as to the best manner of their application, and further extensive and careful investigation is needed before they may be introduced freely into general use.

It must be remembered that in many forms of tuberculosis, with the drugs now available, the late results of treatment are not superior to established forms of therapy, such as bed rest and collapse therapy. Two deterrents to the use of any antituberculous drug are recognized: toxicity and the emergence of drug-resistant strains of tubercle bacilli.

For the above reasons the committee believes that in general it is desirable to withhold drug therapy if other satisfactory therapy is available. It does not favor drug therapy prior to institutional care or as an alternative to bed rest, collapse therapy, or other surgical treatment.

Streptomycin or its derivative dihydrostreptomycin remains the drug of first choice in the treatment of the various forms of tuberculosis. While the use of this drug alone in treatment may be indicated in certain conditions, the combination of streptomycin with paraaminosalicylic acid appears to delay the emergence of streptomycin-resistant strains of tubercle bacilli and to be more effective therapeutically. For tuberculous meningitis and miliary tuberculosis, streptomycin therapy, preferably in combination with other antituberculous agents, is recommended. Streptomycin with paraaminosalicylic acid appears to be the drug treatment of choice in the acute and progressive forms of pulmonary tuberculosis, tuberculosis of the genitourinary tract, and tuberculosis of bones and joints.

On the basis of information available at present, dihydrostreptomycin appears to show no advantages over streptomycin with regard to therapeutic efficiency. The rate of emergence of resistant organisms has not been delayed by its use.

Paraaminosalicylic acid given alone has limited therapeutic benefit as compared with streptomycin, and its prolonged use may result in the emergence of organisms resistant to the drug. By far the most effective use of paraaminosalicylic acid is in combination with streptomycin.

In the judgment of the committee, further, more extensive research in the bacteriological, pharmacological, toxicological, and other aspects of amithiozone (conteben®) is necessary before its value in the treatment of tuberculosis can be determined. It is not believed that the substance should be generally employed in the treatment of tuberculosis until more definite information is available concerning its limitations and potentialities.

In this report the clinical application of these agents is discussed in some detail.

EUGENE SMITH, Ogden, Utah.

PULMONARY TUBERCULOSIS IN CHILDREN TREATED WITH STREPTOMYCIN. E. T. McENERY, H. C. SWEANY, and G. C. TURNER, Illinois M. J. **97**:15 (Jan.) 1950.

This is a report of 25 cases of primary pulmonary tuberculosis in which the patients were treated with streptomycin at the Chicago Municipal Tuberculosis Sanitarium. Twenty-two of the patients were classified as having progressive primary lesions. The ages varied from 8 months to 15 years.

All the patients were observed from two to 36 months. All the criteria for a diagnosis of an active pulmonary process were present before streptomycin administration was started. The dosages used were 0.5 gm. or 0.3 gm. daily. Sixteen cases received the drug for 120 days, and nine were treated for 90 days. No toxic reactions were noted.

Criteria for discharge from the sanitarium consisted of two consecutive gastric washings and one bronchoscopic aspiration, both negative on smear and culture for tubercle bacilli. All but four of the 25 patients were converted to sputum negative. Two of the remaining positive cases have been of the adult type and two of the progressive primary.

BARBOUR, Peoria.

STREPTOMYCIN IN PULMONARY TUBERCULOSIS IN CHILDREN. WILLIAM BERENBERG, CHARLES D. COOK, and CLAIRE W. TWINAM, J. A. M. A. **145**:1044 (April 7) 1951.

Twenty-seven patients with pulmonary tuberculosis were treated with streptomycin intramuscularly in daily doses of 30 to 50 mg. per kilogram of body weight, not exceeding 1.0 gm. daily, for a period of 91 days. No deafness or serious toxicity was encountered. The treatment was found to be of particular value in children ill with relatively recent tuberculous pulmonary

infections of an exudative or pneumonic type. It is of doubtful value in older children ill with fibrocaseous pulmonary tuberculosis of long standing. Paraaminosalicylic acid seems to be the drug of choice as adjunctive therapy and thiazolsulfone when the infection is miliary or meningeal.

KIMBALL, Evanston, Ill.

COCCIDIOIDOMYCOSIS IN CHILDREN. CHESTER I. MEAD, J. A. M. A. **146**:85 (May 12) 1951.

Coccidioidomycosis is a disease entity that has only recently become important as a diagnostic problem in children. The disease was first recognized in Kern County in California in 1901. It is commoner in the summer, when there is exposure to the soil and dust which contains the causative fungus, C. immitis. In children the disease resembles upper respiratory tract infections, influenza, or atypical pneumonia. There are no reliable tests for the acute phase. Skin testing helps in screening after the second or third week. The precipitation test becomes positive the first or second week, the complement fixation test later. Sputum examination and cultures are usually unreliable.

KIMBALL, Evanston, Ill.

A COCCIDIOIDIN PATCH TEST. ROBERT COHEN and MYRNIE A. GIFFORD, J. Pediat. **35**:601 (Nov.) 1949.

The authors tested 120 patients with positive reactions to coccidioidin with a filter paper method similar to that of the Vollmer tuberculin patch test. Only 22.5% showed positive reactions. With an ointment method, only 4% showed positive reactions.

MACDONALD, Pittsburgh.

COMPLEMENT FIXATION TEST IN TOXOPLASMOSIS AND PERSISTENCE OF THE ANTIBODY IN HUMAN BEINGS. ALBERT B. SABIN, Pediatrics **4**:443 (Oct.) 1949.

An antigen prepared from Toxoplasma-infected chorioallantoic membranes, improved by centrifugation at 13,000 rpm for one hour, which removed a nonspecific component capable of fixing complement with certain normal serums, proved to be the preparation of choice for toxoplasmic complement fixation tests. Although it was possible to prepare an antigen of similar potency from mouse brain, the yield from one egg is at least 10 times more than from one mouse. The peritoneal exudate of mice freed of Toxoplasma and cells contains eight times as much antigen a unit volume as a 20% extract of mouse brain or chorioallantoic membranes, but its anticomplementary properties, which cannot be removed by high-speed centrifugation, can be eliminated only by extensive dilution. The highly centrifuged and diluted peritoneal exudate, however, still contains a component which fixes complement with certain normal human serums. Sixteen children, aged 5 weeks to 11 years, with clinically recognized congenital toxoplasmosis and 17 mothers with inapparent or clinically unrecognized infection except for having given birth to children with proved toxoplasmosis were investigated for the presence and persistence of complement fixation antibodies. With the improved antigen and the standardized method that was used, even titers of 1:2 and 1:4 were significant and invariably associated with toxoplasmic-neutralizing antibodies. The serum of all 17 mothers gave positive complement fixation reactions, with titers from 1:4 to 1:64, the higher titers predominating during the first two years after the delivery of the infected child. The serum of 14 of the 16 children (87.5%) with clinical evidence of congenital toxoplasmosis, confirmed by neutralization tests, gave positive complement fixation reactions, with titers ranging from 1:2 to 1:128, the higher titers again predominating during the first two years after birth. One of the two negative reactions was in a 5-week-old child with active infection who died three days after the serum was obtained; it was associated with a high (1:4,096) dye test titer for neutralizing antibody in the infant's serum and a similar dye test titer (1:4,096) and a complement fixation titer of 1:32 in the serum of the infant's mother. The other negative result, in a 7-year-old child with a dye test titer of 1:16, is believed to represent an instance of disappearance of complement fixation antibody after an interval of seven years. Not one serum obtained from 24 children with congenital ocular or neurologic disturbances, or both, not due to toxoplasmosis gave a positive complement fixation reaction with the toxoplasmic antigen; however, among 20 of their mothers, there were four serums with positive reactions, with titers of 1:2, 1:2, 1:8, and 1:16. Toxoplasmic com-

plement fixation antibody can persist for at least six years, and in some instances even longer, in persons with clinically recognized infections as well as in persons with inapparent or clinically unrecognized infections. Since at least seven of the mothers who gave birth to children with congenital toxoplasmosis subsequently gave birth to normal children at a time that the complement fixation antibody titers in some of them were still high (32, 32, 32, 16, 8, 4, 4), it is clear that this antibody can persist in persons in whom the infection has been eradicated or suppressed sufficiently to prevent its congenital transmission.

FROM THE AUTHOR'S SUMMARY.

THERAPY OF TUBERCULOSIS IN INFANTS AND CHILDREN. R. H. HIGH, Pediatrics **7**:215 (Feb.) 1951.

Streptomycin, or dihydrostreptomycin, along with other agents, such as thiazolsulfone (promizole®) or paraaminosalicylic acid, is of value in the treatment of serious forms of tuberculosis in infants and children. Progressive pulmonary tuberculosis and miliary tuberculosis seem to respond most satisfactorily. Tuberculous meningitis has a serious prognosis, but some patients apparently have this infection arrested.

The use of streptomycin for patients with forms of tuberculosis which have a good prognosis without treatment is not recommended. The potential toxicity of the drug and the possible emergence of streptomycin-resistant tubercle bacilli are the major reasons for this recommendation.

FROM THE AUTHOR'S SUMMARY.

PENICILLIN IN THE TREATMENT OF PRENATAL SYPHILIS. E. A. MORGAN, Canad. M. A. J. **61**:275 (Sept.) 1949.

Penicillin therapy in the early stages of prenatal syphilis appears to be superior to all other forms of treatment. In older children, however, this treatment has been unsatisfactory and in no way superior to the older methods. It is felt that further experiments need to be made in dosage schedules and drug combinations before an authoritative statement can be made concerning treatment of older children.

McGUIGAN, Evanston.

CONGENITAL TUBERCULOSIS. H. E. ROBERTSON and C. F. SULLIVAN, Canad. M. A. J. **63**:361 (Oct.) 1950.

A case of congenital tuberculosis is reported. Attention is called to the fact that pulmonary involvement may be due to hematogenous spread from the umbilical vein and ductus venosus.

McGUIGAN, Evanston, Ill.

INTERSTITIAL KERATITIS TREATED WITH CORTISONE. A. K. GEDDES and M. FRANCES MCCALL, Canad. M. A. J. **63**:601 (Dec.) 1950.

The authors describe a case of interstitial keratitis due to congenital syphilis in a 10-year-old child. Treatment with penicillin and cortisone appeared to give more rapid improvement than would have been expected with penicillin alone.

McGUIGAN, Evanston.

STREPTOMYCIN IN THE TREATMENT OF TUBERCULOSIS IN CHILDREN UNDER THE AGE OF TWO YEARS: A SERIES OF 21 CASES. H. G. RISCHBIETH, Clin. Rep. Adelaide Child. Hosp. **1**:211 (May) 1949.

In 41 cases of childhood tuberculosis occurring prior to May, 1947, 16 patients died, making a mortality rate of 39%. Since that time, 21 patients have been seen and all have been treated with streptomycin, with no deaths. In no case did meningitis, miliary tuberculosis, or tuberculous bronchopneumonia develop, despite the fact that 10 children had measles and two whooping cough while they were under observation.

McGUIGAN, Evanston.

A CASE OF MILIARY TUBERCULOSIS AND TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. R. L. THOROLD GRANT, Clin. Rep. Adelaide Child. Hosp. **1**:225 (May) 1949.

Apparent cure is reported in a 4½-year-old boy after streptomycin treatment. Fourteen months after the diagnosis was made the child was apparently normal in every way.

McGUIGAN, Evanston.

BCG VACCINE—ITS EFFICACY AND DISADVANTAGES. B. B. MUKHERJEE, J. Indian M. A. **18**:467 (Sept.) 1949.

The safety of BCG vaccine being considered proved, it is felt by the author that BCG vaccination confers a definite and significant immunity, though the degree and duration of such immunity is not known. Disadvantages rest in the rigid technique necessary to produce the vaccine and the need for using it within two weeks after preparation. The author feels that in a country like India BCG vaccination may prove to be of outstanding value as a control of tuberculosis.

McGUIGAN, Evanston, Ill.

TREATMENT OF CONGENITAL SYPHILIS IN INFANTS. D. N. CHATTERJI, Indian J. Pediat. **18**:82 (April) 1950.

Three series of patients were treated, one with acetarsone, one with penicillin, and one with penicillin preceded by injection of vitamin A. Results were poor in the first two groups. In those given vitamin A the immediate response was gratifying. The author suggests that the syphilitic liver is unable to handle a normal load, besides being deficient in vitamin A. He recommends several doses of 1,000,000 units of vitamin A in addition to total dosage of 50,000 units of penicillin per pound followed by acetarsone.

McGUIGAN, Evanston, Ill.

TUBERCULOSIS OF JOINTS AND SEROUS MEMBRANES: TREATMENT WITH LOCAL ALKALINIZATION AND STREPTOMYCIN. D. H. P. STREETEN, South African M. J. **23**:800 (Sept. 24) 1949.

Patients with tuberculous arthritis, pericarditis, empyema, and peritonitis were treated by local instillation of sufficient alkali (N/20 sodium hydroxide solution) to produce a pH of 9.0, followed by a local injection of streptomycin. A small series of cases produced sufficiently striking results to make it appear that this method is both desirable and advantageous.

McGUIGAN, Evanston, Ill.

BACILLUS OF CALMETTE AND GUERIN (BCG). S. J. FLEISHMAN, South African M. J. **23**:806 (Sept. 24) 1949.

A brief review of BCG vaccination is presented, with a recommendation that it be widely employed for South African natives.

McGUIGAN, Evanston, Ill.

THE EFFECT OF SYPHILIS ON THE OUTCOME OF PREGNANCY IN THE NATIVE. S. B. SACHS, South African M. J. **25**:255 (April 14) 1951.

A survey of 1,329 pregnancies of native mothers free from syphilis and of a similar number suffering from latent syphilis revealed a loss of fetal and early infant life of 7.4% due to syphilis.

McGUIGAN, Evanston, Ill.

CONGENITAL TOXOPLASMOSIS. PAULINE KLENRMAN, South African M. J. **25**:273 (April 21) 1951.

A case of toxoplasmosis in a 6-week-old infant is reported. He had begun showing symptoms of illness at 1 week. Symptoms were suggestive of tuberculous meningitis, the diagnosis being made post mortem. No previous cases had occurred in South Africa.

McGUIGAN, Evanston, Ill.

UNUSUAL ONSET OF TUBERCULOSIS IN INFANTS. A. GYLLENSWARD, Pédiatrie **37**:127 (Jan.-Feb.) 1948.

A 3-month-old boy was sent to the hospital for BCG vaccination because open tuberculosis was discovered in his mother. He was separated from his mother 12 days before admission to the hospital. On admission physical examination revealed a healthy, well-nourished boy; roent-

genograms of the chest and Mantoux reaction (1 mg.) were negative; the sedimentation rate was normal, and gastric lavage showed no unusual results. Five weeks after the last exposure, the sedimentation rate began to rise, there was no elevation of temperature, and gastric lavage samples showed tubercle bacilli by culture as well as by guinea pig inoculation. It was not until two to three weeks later that the Mantoux reaction and the roentgenographic study became positive. Similar observations by other authors are reviewed in this article.

GLASER, Chicago.

STATUS OF THE UNSATURATED FATTY ACIDS IN CHILDREN WITH TUBERCULOSIS. B. CARLETTI, Minerva pediat. **1**:252 (July) 1949.

The unsaturated fatty acids in the bloods of 17 children with tuberculous infections were found to be below the normal figures in each case. Findings are similar for allergic patients; these allergic patients have been benefited by being fed unsaturated fatty acids. It is suggested that similar feedings may be beneficial to tuberculous patients.

HIGGINS, Boston.

STREPTOMYCIN IN ACUTE PULMONARY TUBERCULOSIS. D. VUGA, Minerva pediat. **1**:276 (July) 1949.

Constant and favorable results followed administration of streptomycin to 16 patients with acute, febrile tuberculosis, several in immediate danger of dying. Such cases included disseminated bronchopneumonia, confluent bronchopneumonia, caseous pneumonia, and aspiration pneumonia following hemoptysis.

HIGGINS, Boston.

STREPTOMYCIN TREATMENT FOR EXUDATIVE PERIFOCAL TUBERCULOSIS IN CHILDREN. U. VIGNOLO-LUTATI, Minerva pediat. **2**:467 (Oct.) 1950.

Twenty-one of 24 children with tuberculous pulmonary infiltration responded favorably to streptomycin therapy. The clinical results were much better than was the case in the prestreptomycin years.

HIGGINS, Boston.

HEMOLYTIC TENDENCIES AND BONE MARROW FINDINGS IN CHILDREN UNDER TREATMENT WITH PARAAMINOSALICYLIC ACID (PAS). E. DEPPERU and M. RICCARDI, Pediatria **58**:184 (March) 1950.

In a study of seven children with tuberculosis it was observed that the giving of paraaminosalicylic acid increased the fragility of the red blood cells and led to positive reaction to an indirect van den Bergh test and urobilinuria. It also caused increased myelocytic activity in the bone marrow.

HIGGINS, Boston.

FUNCTIONAL HYPOGALACTIA AND MARCONI THERAPY OF DIENCEPHALON AND HYPOPHYSIS. STEVERINO PEDONE, Riv. clin pediat. **48**:649 (Oct.) 1950.

The author reviews the factors which determine the activity of the mammary glands and gives the proper importance to the stimulating action of the diencephalon on lactation and especially of the hypophysis (which secretes the prolactinic hormone) and describes the physical-biological properties of Marconi therapy.

He has treated 19 patients with functional hypogalactia with Marconi therapy (ultrashort waves) of the diencephalon-hypophysis region. Good results were obtained in 17 of the 19 cases, only in women in the puerperal period or in the initial stage of breast feeding, when other means and other kinds of Marconi treatment (in mammary regions) might have given relatively good results, but also some months after breast feeding had begun (in the sixth and seventh months) when all the therapeutic means used till then had not been of much use. No positive results were obtained in two of the 19 patients, as one was a woman already treated with electric shock and the other a woman affected by alterations of the endocrine system.

FROM THE AUTHOR'S SUMMARY.

ACTUAL TREATMENT OF TUBERCULOSIS MENINGITIS AND RESULTS OBTAINED IN CHILDREN'S HOSPITAL OF ZURICH. E. ROSSI and F. PERABO, Acta pediat. españ. **88**:407 (April) 1950.

Rossi and Perabo from Zurich, Switzerland, report on a study of 46 children treated over a period of three years with streptomycin and paraaminosalicylic acid (crystallized with a pH of 7.35; proprietary name "Nahiumsals").

No case was considered too advanced, and even apparently moribund patients were treated. Of course, better results were obtained when diagnosis was made early. In each case the tubercle bacilli either were present in the spinal fluid of the patient, or were recovered from an experimental animal inoculated with the spinal fluid.

There are three methods of administering streptomycin at Zurich: (1) in large doses; (2) small doses in short time and at long intervals; (3) small doses over a long period of time.

Charts show the results in each type of treatment. Seven children treated by the first method died; of the seven treated by the second method, five died, and two are still living, with supervision after more than one year.

The best results were obtained by the third method. Of 29 patients treated with small doses over a long period, 18 had apparent cures or were very much improved and 11, or 34%, were unaffected by the treatment. Twenty of the total 46 are still living and under observation now; six of the 20 are clinically well with spinal fluid negative for tubercle bacilli; five are clinically well but have a positive colloidal gold curve. Another three of the 20 still have an abnormal spinal fluid and clinical defects as well. Five have normal spinal fluid but defective neurological symptoms. Four had ataxia; two had spastic paralysis; and one of these two has a psychosis. One patient had motor manifestations only, with good intelligence. Finally, one child showed a paralysis of the medullary section of the cord with all classic symptoms. She was at first treated only with paraaminosalicylic acid. Dr. Weber performed a laminectomy in the neurosurgical division. The tuberculous process was at the level of the first lumbar vertebra. This made the intrathecal administration of streptomycin unwise. After the operation, paraaminosalicylic acid was discontinued and streptomycin substituted.

The routine of the medication follows: 1. Streptomycin was given intrathecally for the first two weeks, 1 to 2 mg. per kilogram of body weight daily. Lumbar and cisternal punctures were alternated; no catheters were used in their technique.

2. In the next week the dosage varied with the development and gravity of the illness; at least 1 mg. was given, but with only one puncture daily.

3. After the first month spinal punctures was done only three times a week; then after the third month, twice a week; and thus until the spinal fluid was negative for tubercle bacilli.

The streptomycin is given at body temperature with 10 mm. per cc. If a cisternal puncture is done only half of the usual dosage is given.

The doctors believe that spinal injections are much more effective than intramuscular ones. They determine the beginning of a block by the albumin in the spinal fluid rather than by the amount of streptomycin in the lumbar and cisternal fluid.

If given intramuscularly, 30 to 40 mg. per kg. is administered daily for a month. The total must not be more than 500 mg. or 0.5 gm. This is also given until the spinal fluid is free of pathogens.

Paraaminosalicylic acid is given in doses of 0.5 gm. per kg. body weight daily for six days. To alleviate secondary symptoms—anorexia, vomiting—a rest may be given after the fourth day. The drug may be given intravenously, intrathecally, or even orally in sugar-coated masses called "sugar plums." The granulated form is good for the nursing child and an adequate blood level is maintained; it is rapidly eliminated with the cessation of medication.

ALLEN, Santa Fe, N. M.

TREATMENT OF SCROFULA WITH BISMUTH. NOACK, Monatsschr. Kinderh. **97**:197 (Aug.) 1949.

Scrofula consists of chronic rhinitis, edema of the skin (habitus pastosus), phlyctenular keratoconjunctivitis, blepharospasm, and eczematous lesions around the eyes, nose, and mouth and occurs in tuberculous children with a lymphatic-exudative diathesis. The most characteristic

lesion is the phlyctenular keratoconjunctivitis. Intramuscular injections of bismuth were found to be of value in clearing the lesions of scrofula in nine patients, none of whom showed subsequent exacerbations. One patient with desquamative erythroderma (Leiner's disease) and 17 patients with tuberculous phlyctenular keratoconjunctivitis were also benefited by this treatment.

HARTENSTEIN, Chicago.

DIFFERENTIAL ERYTHROCYTE SEDIMENTATION RATE IN THE DIAGNOSIS OF SYPHILIS: A PRELIMINARY REPORT. H. L. SUN and C. K. HU, Chinese M. J. **69**:46 (Jan.-Feb.) 1951.

The Bergamasco method for determining the erythrocyte sedimentation rate was modified for use as a syphilis test. The method used was as follows: 1. Two cubic centimeters of fresh blood was added to 0.5 cc. of sodium citrate solution in a centrifuge tube and mixed thoroughly for two minutes. 2. To each of two test tubes 1.2 cc. of citrated blood was added. The first contained 0.1 cc. of a 1:10 dilution of the Kahn-test antigen; the second, 0.1 cc. of isotonic sodium chloride solution. The contents of each tube were mixed for two minutes. 3. The contents of the two tubes were separately transferred into two Westergren tubes up to 200 mm. in height. The tubes were then placed firmly in a rack. Results were read at the end of two hours. If the sedimentation rate of the antigen-blood sample exceeded that of the control (isotonic-sodium-chloride-blood) by more than 2 mm., the result was interpreted as positive for syphilis.

In 231 observations this test was comparable to the Wassermann in accuracy.

MACDONALD, Pittsburgh.

BOVINE TUBERCULOSIS IN MAN IN SWEDEN. ERIC HEDVALL, Nord. med. **42**:1215 (July 22) 1949.

Definite or suspected cases of milk-borne bovine tuberculosis are reported to the ministry of health, and veterinary examination of the cattle of the particular farm from which the milk is delivered is done. The ministry of health reports cases of tuberculosis involving udder in cattle to the nearest tuberculosis dispensary through which examinations of persons who have ingested the milk from the diseased cow are carried out. Sale of unpasteurized milk is forbidden in cities and rural districts. The method of Bang and Ostertag has been used to great advantage in stamping out tuberculosis in cattle. Since 1914 Sweden has been divided regarding bovine tuberculosis into three areas, tuberculosis-free, protected, and other areas. For the first area there is a provision requiring the reporting of every new discovered case of bovine tuberculosis and compulsory tuberculin testing and compulsory slaughter of animals showing tuberculosis. The import of cattle that have not been controlled in respect to tuberculosis is forbidden. The tuberculosis-free area at present comprises nearly 72% of the country. In the remaining area nearly 90% of the cattle are under tuberculosis control. Bovine tuberculosis in Sweden is now rapidly regressing, and in the near future will in all probability cease to be an important source of infection in man.

WALLGREN, Stockholm, Sweden.

CONGENITAL TOXOPLASMOSIS. TAGE HÖGLUND, Nord. med. **44**:1104 (July 7) 1950.

Höglund reports a case of a 9-year-old girl with pubertas praecox, hydrocephalus, amaurosis (chorioretinitis), and imbecility. The neutralization reaction was positive in 1:250 to 1:1,250 dilutions. The reaction for the mother was positive in 1:50 to 1:1,250 dilutions. The father used to kill rabbits that the mother had to skin and prepare.

WALLGREN, Stockholm, Sweden.

REMARKABLE COURSE OF BCG VACCINATION IN A NEWBORN CHILD WITH SUBCUTANEOUS FAT NECROSIS. GERT VON SYDOW, Nord. med. **44**:1324 (Aug. 18) 1950.

A boy who had weighed 5,150 gm. and been slightly asphyxiated at birth was given an intradermal injection of BCG vaccine on the seventh day of life. Five weeks later suppuration appeared at the site of inoculation. Eleven weeks after inoculation a large abscess was opened in a regional lymph node. Avirulent tubercle bacilli of BCG type were cultivated both from the inoculation abscess and from the abscessed lymph node. Splenomegaly was observed 11

weeks after the inoculation. There were increased sedimentation rate and slight anemia. The child displayed subcutaneous fat necrosis, and it is suggested that the abscess formation was due to the injection's having been made into a part of the skin that was the site of such a fat necrosis.

WALLGREN, Stockholm, Sweden.

Diseases of Blood, Heart and Blood Vessels, and Spleen

CONGENITAL HEMOLYTIC JAUNDICE IN A NEGRO FAMILY. J. CHURG and M. ROSENBAUM, Am. J. M. Sc. **217**:383 (April) 1949.

Three typical cases of congenital hemolytic jaundice were encountered in a Negro family consisting of 10 persons. In two of the patients, the mother, age 38, and a daughter, age 9 years, the disease was very severe, accompanied with hemolytic crises and typical roentgenographic changes in the bones of the skull. In the third case, of a daughter, age 5 years, there were typical blood changes but as yet few clinical manifestations. Review of the literature shows that congenital hemolytic jaundice is very rarely found in the Negro race.

HENSKE, Omaha.

CALCIFICATION OF THE MYOCARDIUM: A PATHOLOGIC STUDY OF THIRTEEN CASES. IRA GORE and WALTER ARONS, Arch. Path. **48**:1 (July) 1949.

Of the 13 cases of calcification of the myocardium taken from the material at the Army Institute of Pathology, all patients are adults except one, a 4-month-old white boy in whom there was a history of excessive intake of vitamin D. At autopsy cardiac lesions as seen in the adults, consisting of calcium deposits laid down on necrotic muscle fibers, were shown. The basis for muscle necrosis was the ischemia secondary to medial calcification of the coronary arteries with coronary thrombosis. In this case the excess vitamin D intake provided a condition in which there was an augmented and accelerated tendency toward the development of dystrophic calcification. The process in the heart muscle in such an instance is regarded, therefore, as an example of accelerated dystrophic mineralization. Widespread deposits of calcium were found elsewhere in other organs in this case.

HAW CHAN, San Francisco.

DOUBLE AORTIC ARCH. WILLIS J. POTTS, STANLEY GIBSON, and ROBERT ROTHWELL, Arch. Surg. **57**:227 (Aug.) 1948.

The clinical picture of this anomaly is rather characteristic. Laryngeal stridor and difficult respiration are usually the first symptoms which indicate to the mother that all is not well with her child. These symptoms appear shortly after birth, may be relatively mild or severe, are often intermittent, and at times vary with the position in which the infant is placed. Respirations are usually rapid and noisy, and even during sleep breathing is labored. Asthma-like wheezing can be heard in the chest. Attacks of severe dyspnea are frequently associated with cyanosis and suprasternal retraction. Spells of unconsciousness are not uncommon. Recurrent infections of the upper part of the respiratory tract, bronchitis, and pneumonia keep the child in a poor state of health. As the child grows older, a crowing, nonproductive cough, like the bark of a sea lion, is characteristic. These symptoms are not unlike those ordinarily ascribed to an enlarged thymus. The suspected diagnosis is confirmed by fluoroscopic and roentgen examinations. Administration orally of barium sulfate or iodized poppy-seed oil will help to show a concave defect in the esophagus produced by pressure of the abnormal vessel. Two cases of double aortic arch are reported in which treatment was surgical.

KAISER, Rochester, N. Y.

PHOTOMETRIC MEASUREMENT OF PLASMA pH. D. D. VAN SLYKE, J. R. WEISINGER, and K. K. VAN SLYKE, J. Biol. Chem. **179**:743 (June) 1949.

A method is described for the measurement of plasma pH which utilizes as little as 0.2 ml. of plasma. The method involves the dilution of the plasma with suitable phenolsulfonphthalein (phenol red) solutions and observation of the resultant optical density (at 38 C.) in a suitable spectrophotometer at 550 mm. The curve of optical density versus pH is practically linear

throughout plasma pH range. A check of 26 plasma samples of widely varying pH with the hydrogen electrode revealed that the photometric method gave results averaging 0.002 pH unit higher. The standard deviation of the difference obtained by the two methods was 0.022 unit, and the maximal deviation was 0.04 unit.

FORBES, St. Louis.

SURGICAL CORRECTION OF A DOUBLE AORTIC ARCH. WALTER F. BUGDEN, J. Thoracic Surg. **20**:928 (Dec.) 1950.

This condition was first described by Hammel, in 1737. Since that time over 40 cases have been reported in the literature. A double aortic arch is due to the persistence of both fourth branchial arches, forming a vascular ring around the esophagus and trachea.

Infants with this congenital disorder may have noisy, stridorous respirations, often noted soon after birth. Feedings may be slow and accompanied with respiratory embarrassment. Episodes of respiratory infection are frequent. However, the presence of a double aortic arch without symptoms is usually not an indication for surgical intervention.

The author reports a case of this type; it was correctly diagnosed prior to surgery, and treatment by resection of the anterior arch was successful.

MEYER, Chicago.

CONGENITAL ABSENCE OF THE PERICARDIUM. B. G. P. SHAFIROFF, J. Thoracic Surg. **21**:30 (Jan.) 1951.

Over 80 cases of congenital deficiency of the pericardium have been reported in the literature. The anomaly has occasionally been noted at the time of surgery. The case reported is of a 12-day-old infant who died of cerebral injury occurring at the time of delivery. Examination of the thoracic cavity showed a complete absence of the pericardium, although the heart maintained its normal position in relation to the mediastinum. The heart, which lay in a common serous cavity with the left lung, was entirely covered by epicardium. The left phrenic nerve followed a normal anatomical course in the neck, entered the thorax behind the left innominate vein, crossed in front of the aortic arch, and followed along the rudimentary pericardial fold along the right border of the heart. The pericardiophrenic branch of the internal mammary artery was absent on the left side. The right phrenic nerve followed the normal course. Absence of the pericardium apparently does not produce symptoms or marked changes in cardiac function.

MEYER, Chicago.

ANOMALOUS ORIGIN OF THE LEFT CORONARY ARTERY FROM THE PULMONARY ARTERY (BLAND-WHITE-GARLAND SYNDROME). BENJAMIN M. GASUL and ERNEST LOEFFLER, Pediatrics **4**:498 (Oct.) 1949.

A review of the literature and four cases of cardiac hypertrophy due to an anomalous origin of the left coronary artery from the pulmonary artery in infants are given. The diagnosis is based upon a history of an apparently normal birth and normal development until 2 to 3 months of age, when "colicky" pains coming on usually during or soon after feedings take place and examinations reveal an enlarged heart but no cyanosis or murmurs. The enlargement is due to the dilatation of the left ventricle which can be best appreciated by fluoroscopic examination in the left anterior oblique view. In this view the inflow tract of the left ventricle is seen to be definitely enlarged, and no matter how much the patient is rotated, it is difficult to find the left ventricle clearing the spine. In some cases an aneurysmal dilatation of the left ventricle takes place, and the electroencephalogram shows low-amplitude QRS complexes and inversion of the T waves but no axis deviation. This syndrome can be differentiated from all other conditions causing cardiac enlargement in infancy by the criteria presented.

FROM THE AUTHORS' SUMMARY.

SPHEROCYTOSIS AND INCREASED FRAGILITY OCCURRING IN ERYTHROBLASTOSIS FETALIS ASSOCIATED WITH ABO INCOMPATIBILITY. G. C. ROBINSON, RUTH M. PHILLIPS, and M. PRYSTOWSKY, Pediatrics **7**:164 (Feb.) 1951.

Four cases of erythroblastosis fetalis secondary to maternal A-B-O isoimmunization are reported. In each instance spherocytosis and increased fragility to hypotonic saline occurred during the phase of hemolysis.

Clinically each case was represented by anemia, jaundice, splenomegaly, and hepatomegaly. Reticulocytosis and an increase in nucleated red blood cells were part of the blood picture. None of the patients showed Rh or Hr incompatibility.

Findings highly suggestive of A-B-O isoimmunization were the rise in appropriate maternal antibody titer postnatally and the presence of immune antibodies in three of the four infants' serums. Spherocytosis and increased fragility to hypotonic saline occurred in each of the four infants, the latter lasting longer than the former.

Each patient required only a minimum of small blood transfusions.

FROM THE AUTHORS' SUMMARY.

ACUTE HEMOLYTIC ANEMIA RELATED TO NAPHTHALENE. W. B. SCHAFER, Pediatrics **7**:172 (Feb.) 1951.

A case of acute hemolytic anemia in a newborn infant, apparently due to naphthalene poisoning, is reported. It is thought that absorption through the oiled skin occurred after repeated exposure to diapers which had been stored in naphthalene mothballs and moth crystals.

FROM THE AUTHOR'S SUMMARY.

ENDOCARDIAL FIBROELASTOSIS. FRED C. COLLIER and PAUL D. ROSAHN, Pediatrics **7**:175 (Feb.) 1951.

Eleven cases of fibroelastosis of the endocardium are reviewed, and two new cases are reported. The microscopic evidence of hyperplasia of the fibrous and elastic tissue elements of the endocardium in the two new cases reported parallels the findings in the previously reported cases. The pathogenesis of this lesion is at present not clear, but it is possible that the explanation lies in a developmental aberration in the fetus resulting from maternal disease during the gestation period.

FROM THE AUTHORS' SUMMARY.

BROCK PROCEDURE FOR THE RELIEF OF PULMONARY STENOSIS IN THE TETRALOGY OF FALLOT. D. F. DOWNING, C. P. BAILEY, and R. P. GLOVER, Pediatrics **7**:230 (Feb.) 1951.

The surgical relief of pulmonary stenosis has been both direct and indirect. The indirect procedures have inherent dangers because of the fact that an arteriovenous shunt is created; the direct approach of Brock appears to be without these dangers, and the circulation to the lungs is allowed a normal course.

This approach entails an incision into the right ventricular chamber and the cutting of the stenosed pulmonary valve or the removal of obstructing tissue in the ventricular outflow tract. Cyanosis is usually relieved immediately, and the patient's exercise tolerance approaches that of a normal person.

Eight case reports are presented. There was one fatality.

FROM THE AUTHORS' SUMMARY.

TRICUSPID ATRESIA: REPORT OF THREE CASES AND EVALUATION OF DIAGNOSTIC CRITERIA. H. L. ABRAMS and R. H. ALWAY, Pediatrics **7**:660 (May) 1951.

Congenital tricuspid atresia or stenosis is a form of cyanotic heart disease which may be alleviated by establishing a communication between the pulmonary and the systemic circulation. Review of the literature reveals that this anomaly is usually characterized by cyanosis, present at birth and persistent; systolic murmurs, which are not diagnostic; elevated hemoglobin; left axis deviation on the electrocardiogram, and roentgenologic evidence of a small right ventricle and a large left ventricle. Angiocardiography shows sequential opacification of the right atrium, left atrium, and left ventricle, without evidence of significant right ventricular opacification.

Three previously unreported cases of congenital tricuspid atresia or stenosis are presented, in one of which no axis deviation was present, and the roentgenologic findings were compatible with right ventricular enlargement. In this case angiocardiographic studies suggested the diagnosis.

The combination of a cyanotic congenital cardiac anomaly and left axis deviation is not pathognomonic of tricuspid atresia, since this combination has been found in transposition of the great vessels, truncus arteriosus, the tetralogy of Fallot with associated atrial septal defect, and the tetralogy of Fallot with patent ductus arteriosus. Conversely, left axis deviation is not always present in cases of tricuspid atresia. Similarly, the routine roentgenologic examination may obscure the presence of an underdeveloped right ventricle. In doubtful cases angiocardiography may offer the only method of establishing the diagnosis.

FROM THE AUTHORS' SUMMARY.

PREVALENCE OF HEART DISEASE IN TORONTO CHILDREN: 1948-1949 CARDIAC REGISTRY. J. H. GARDINER and J. D. KEITH, Pediatrics **7**:713 (May) 1951.

A cardiac registry was established in Toronto for the purpose of recording useful data regarding heart disease in the children of the city.

The prevalence of heart disease in school children was found to be 0.37%, with 55% of cases due to congenitally deformed hearts and 44% due to rheumatic heart disease. In the age group from birth to 15 years congenital heart disease was found twice as commonly as rheumatic heart disease. Deaths from congenital heart disease were roughly six times as common as deaths due to rheumatic heart disease. The frequency of congenital abnormalities according to the cause of death showed that tetralogy of Fallot was first, transposition of the great vessels second, anomalies of the aortic valve and ascending aorta third. Thus, efforts might well be directed toward evolving satisfactory methods of treating transposition of the great vessels, the second most frequent cause of death from congenital heart anomalies.

FROM THE AUTHORS' SUMMARY.

THE INHERITANCE OF SICKLE CELL ANEMIA. JAMES V. NEEL, Science **110**:64 (July 15) 1949.

The author reviews the two hypotheses which have been suggested as an explanation for the inheritance of sickle cell anemia. In a test of 42 parents of 29 patients with the disease every parent exhibited the sickling phenomenon. With the use of this data, and by argument from genetic theory, the author rejects the variable dominant hypothesis and concludes that the homozygous-heterozygous hypothesis is correct. The latter states that a heterozygous person will show sicklemia only, whereas the homozygote will exhibit sickle cell anemia.

FORBES, St. Louis.

IRON METABOLISM: HEME SYNTHESIS IN VITRO BY IMMATURE ERYTHROCYTES. R. J. WALSH, E. D. THOMAS, S. K. CHOW, R. G. FLUHARTY, and C. A. FINCH, Science **110**:396 (Oct. 14) 1949.

Whereas there is an apparent lack of exchange of iron between the mature erythrocyte and surrounding plasma, reticulocytes will readily assimilate radioactive iron and synthesize heme in vitro. In the case of normoblasts, iron uptake is even greater. Ferrous iron is taken up more rapidly than ferric; iron uptake is impaired at low temperatures and by lack of glucose.

FORBES, St. Louis.

PATENT DUCTUS ARTERIOSUS. V. O. HERTZMAN and S. F. STRONG, Canad. M. A. J. **61**:495 (Nov.) 1949.

The importance of accurate diagnosis of patent ductus arteriosus is pointed out. Of 17 patients operated on for this condition, six had no patent ductus arteriosus. Diagnostic points are reviewed.

McGUIGAN, Evanston, Ill.

BLOOD VOLUME STUDIES IN HEALTHY CHILDREN. SHEENAH J. M. RUSSELL, Arch. Dis. Childhood **24**:88 (June) 1949.

Plasma and blood volume investigations have been carried out in 80 healthy children. Increase in age was accompanied with increase in absolute plasma and blood volumes. Unit volumes

related to height and surface area showed a rise with increasing age, while unit volume related to weight remained unchanged.

Of the three measurements, weight, height, and surface area, weight bore the closest relation to both plasma and blood volumes, as judged by the correlation coefficients and the scatter of the results round the regression equations.

Because of the tendency of body weight to undergo rapid change, especially in children, height has been suggested as the most suitable correlation factor when comparing the plasma and blood volumes in disease with those found in health. Both plasma and blood volumes showed a tendency to be higher in boys than in girls of the same size.

KELLY, Milwaukee.

A CASE OF CONGENITAL IDIOPATHIC HYPERTROPHY OF THE HEART. D. J. CONWAY, Arch. Dis. Childhood **24**:198 (Sept.) 1949.

After a short illness with screaming, dyspnea, and anorexia, a child died suddenly from cardiac failure. Postmortem examination showed gross enlargement and hypertrophy of the heart, particularly of the left ventricle. Other systems were normal, except for some bronchitis. Microscopic examination showed that there was gross hypertrophy of individual muscle fibers without any other pathological change in the heart.

KELLY, Milwaukee.

POLYARTERITIS IN CHILDHOOD. A. V. NEALE, Arch. Dis. Childhood **24**:229 (Sept.) 1949.

Some considerations of the possible etiological relations in polyarteritis in childhood are presented, and two cases of the "dermal" form are recorded. A prolonged illness, with an ever-present menace of possible visceral involvement, was successfully negotiated, and clinical recovery without sequelae occurred in one child. In another child the prolonged and variable clinical course seemed to have reached a favorable outcome, but unexpectedly a sudden and intense relapse quickly progressed to acute obliterative cutaneous arteritis and spreading ischemic necrosis.

KELLY, Milwaukee.

MEDICAL ASPECTS OF SPLENECTOMY. H. N. ROBSON, Edinburgh M. J. **56**:381 (Sept.) 1949.

Splenectomy can be an important therapeutic measure when there is a disorder of red cells, white cells, or thrombocytes (platelets). In hemolytic anemia splenectomy removes an important center of destruction of abnormal red cells. In thrombopenia and leucopenia the inhibiting effect of the spleen on the bone marrow is removed. Since our knowledge of the specific influence of the spleen on the various blood elements is incomplete, splenectomy must be regarded as a crude way of altering splenic function.

MACDONALD, Pittsburgh.

CHEMOTHERAPY IN RETICULOSIS. JAMES INNES, Edinburgh M. J. **56**:481 (Oct.) 1949.

Innes reviews recent progress in chemotherapy in some of the disorders of the reticulo-endothelial system. The obvious disadvantages of radiotherapy have led to a search for some simpler method of treatment which will attack neoplastic cells without injuring the cells of normal body tissues. No such agent has yet been found, but considerable progress has been made. There are strong indications that the fundamental difference between normal cells and neoplastic cells lies in processes connected with nucleic acid metabolism. This nucleic acid metabolism is the center piece around which most modern research in this field revolves.

Several drugs are now available. Arsenic, the old timer, sometimes induces remission in chronic myeloid leukemia. Urethan may produce temporary remissions in chronic myeloid and occasionally in chronic lymphatic leukemia and in multiple myeloma. Nitrogen mustard (methyl-*bis* or *tris* [2-chloroethyl] amine hydrochloride) is a temporary palliative in Hodgkin's disease, lymphosarcoma, chronic leukemia, primary polycythemia (polycythemia vera), mycosis fungoides, and primary lung carcinoma. In multiple myeloma 4,4'-stilbenedicarboxamidine ("stilbamidine") may give temporary relief, and 4-aminopteroylglutamic acid ("aminopterin") may produce temporary remissions in certain cases of subacute lymphoblastic leukemia. None of these drugs is curative, and their toxic effects may be quite serious. However, there is hope for the future in this field of research.

MACDONALD, Pittsburgh.

HAEMOPHILIA IN A SOUTH AFRICAN BANTU. S. B. GRIFFITHS and R. LIPSCHITZ, South African M. J. **23**:720 (Aug. 27) 1949.

Hemophilia in a 15-year-old male Bantu is reported, the first in this race and the second recorded in an African native. A brother, a maternal male cousin, and a maternal uncle were known to be bleeders.

McGUIGAN, Evanston, Ill.

BLOOD FINDINGS IN MORBUS CAERULEUS (IRON AND HEMOGLOBIN METABOLISM). A. PRADER and E. ROSSI, Helvet. paediat. acta **5**:159 (May) 1950.

In a large group of children with congenital cyanotic heart disease (morbus caeruleus) the authors found a mean increase in the total hemoglobin of 163% (26.6 gm. per kilogram of body weight), in the serum iron of 123% (201 γ per 100 cc.) and in the serum bilirubin of 198% (1.49 mg. per 100 cc.). The direct van den Bergh reaction was always negative.

Indirect evidence indicates that total body iron, intrinsic and extrinsic iron metabolism, and iron requirement are raised.

There is a rise in the total hemoglobin metabolism, but in proportion to the total hemoglobin the metabolism is normal (based on the reticulocyte count and the rate of urobilin excretion).

The main cause of the raised iron and bilirubin is the increased hemoglobin metabolism. The reduction of the plasma volume and the hypoxic liver damage may play a supporting role. There is no accelerated hemolysis.

Cases with normal or low serum iron are masked iron deficiency anemias. They are characterized by a low color index and a decreased mean corpuscular volume.

A review of literature indicates that the observed changes in the iron and hemoglobin metabolism are probably present in each true polyglobulia (polyglobulia of altitude, polycythemia vera).

FROM THE AUTHORS' SUMMARY.

BLOOD FINDINGS IN MORBUS CAERULEUS (ERYTHROCYTE CHARACTERISTICS). A. PRADER and E. ROSSI, Helvet. paediat. acta **5**:172 (May) 1950.

Prader and Rossi examined 50 children with congenital cyanotic heart disease (morbus caeruleus). Hemoglobin, the number of erythrocytes, and the hematocrit value are strongly increased. Color index is normal. Mean corpuscular volume and mean corpuscular diameter are increased (macrocytosis), mean corpuscular thickness is normal, spherical index is rather decreased (platycytosis). There is anisocytosis but no poikilocytosis. The mean corpuscular hemoglobin is normal, and the mean corpuscular hemoglobin concentration is rather decreased. Maximum osmotic resistance is increased; minimum resistance is decreased.

The polyglobulia often masks an iron-deficiency anemia. In these cases the erythrocytes have most of the signs of an iron-deficient anemia and the usual increase of the amount of iron in the serum is absent.

Nearly the same erythrocytic syndrome as in the blue disease is encountered in other polyglobulias due to lack of oxygen, and in liver diseases.

Lack of oxygen is possibly the direct or indirect (hypoxic liver damage) reason of the changes of the erythrocytes. It may be an adaptation mechanism for a better use of oxygen.

FROM THE AUTHORS' SUMMARY.

BLOOD FINDINGS IN MORBUS CAERULEUS (LEUKOCYTES AND WHITE BLOOD PICTURE). A. PRADER and L. HOLLÄNDER, Helvet. paediat. acta **5**:185 (May) 1950.

The authors examined the number of white blood cells and the white differential count in 41 cases of congenital cyanotic heart disease (morbus caeruleus). They found a slight leucopenia with a slight decrease in the absolute number of eosinophils, monopenia and lymphopenia. Lack of oxygen may be the direct cause, and a hyperfunction of the adrenal cortex (a stage of resistance of the Selye general adaptation syndrome) the indirect cause.

FROM THE AUTHORS' SUMMARY.

ACUTE ERYTHROBLASTOPENIA WITH OCCURRENCE OF ABNORMAL GIANT ERYTHROBLASTS IN BONE MARROW. C. GASSER and W. ADANK, Helvet. pædiat. acta **5** (Supp.):37 (July) 1950.

A short account is presented of four new cases of "acute erythroblastopenia." The authors' observations on the previous ten cases have been confirmed, suggesting that it is a disease of general occurrence, due to a selective interference with normal erythropoiesis. The damage arises probably from a toxic-allergic reaction which is dependent on endogenous, constitutional, and predisposing factors, and oxogenous agents (toxins, drugs, infections, etc.). Acute aplastic erythroblastic crises are the result. This syndrome produces severe anemia only in cases of spherocytic anemia, the erythrocytes having a much shorter life span. The abnormal erythroblasts found in this condition are described in detail with the aid of two plates in color.

FROM THE AUTHORS' SUMMARY.

IMPORTANCE OF SYSTEMATIC PRECORDIAL ELECTROCARDIOGRAPHIC EXAMINATIONS IN RHEUMATIC CARDITIS. L. SALMI, Clin. pediat. **32**:87 (Feb.) 1950.

Salmi speaks of electrocardiographic experience gathered in the last three years with the employment of precordial systematic exploration in acute polyarthritis and fever, and in rheumatic carditis. She emphasizes useful diagnostic elements resulting from the simultaneous employment of standard precordial and unipolar leads, with special regard to the alterations of ventricular repolarization often noted in rheumatic fever, and to the importance of the modifications due to late activation for diagnosis of auricular and ventricular hypertrophy, to overweight, and to block syndromes.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF ANEMIA IN INFANTS AND IN CHILDREN WITH FERRO-REDOXON (IRON ASCORBATE). HANS ZEISEL, Arch. Kinderh. **137**:155 (Sept.) 1949.

Ferro Redoxon (iron ascorbate) is stabilized in the ferro state. The treatment results in 56 infants and children with nutritional or postinfectious anemia were very satisfactory. Daily dosage used was 30 mg. during the first year of life, in older children 60 to 120 mg. iron ascorbate.

ARON, Chicago.

COR TRILOCULARE BIATRIATUM WITH STENOSIS OF THE PULMONARY ARTERY. E. ZDANSKY, Wien. klin. Wchnschr. **63**:144 (Feb. 23) 1951.

A 9-year-old boy who had been severely cyanotic since birth was examined with roentgenography and angiocardiography. The diagnosis was cor triloculare biatriatum with abnormally narrow pulmonary artery arising from a persistent bulbus arteriosus and an aorta arising from the large common heart chamber. The boy was operated on according to the Blalock-Taussig method with good results.

AMBERG, Rochester, Minn.

LEVEL OF CIRCULATING RESERVE PROTEIN IN BLOOD FOLLOWING ADMINISTRATION OF DIFFERENT PROTEIN FOODS. P. UJSAGHY, Pædiat. danub. **6**:259 (Oct.-Dec.) 1949.

The observations were made on 42 infants under 1 year of age, most of them artificially nourished. Part of the group were healthy, while the remainder had recovered from various acute or chronic diseases. Variations of the total protein content of the plasma, following feeding with different casein, albumin, and globulin mixtures, were studied by a special method. It was observed that if the original level of total protein was below 7%, the level could be raised by both albumin- and globulin-containing foods. If the initial level was above 7%, the protein content could be increased only by casein, while it generally suffered a decrease following administration of albumin and globulin. This effort is ascribed to the increase in reserve protein in the circulation.

FROM THE AUTHOR'S SUMMARY.

SURGICAL TREATMENT OF OPEN BOTALLI'S DUCT. H. WAMSTEKER, Maandschr. kindergeneesk. **19**:73 (May) 1951.

Since Gross first closed a patent ductus arteriosus (open Botalli's duct) operatively in 1938 this disease has been generally considered a surgical problem. It is not a congenital malformation of the vessel, but rather a postnatal deficiency of the mechanism of closure. The closure of the open duct causes a considerable decrease in the output of the left ventricle.

The main symptoms are (1) delayed physical development, (2) a low diastolic pressure and a great difference in the pulse pressure, and (3) a "machinery murmur," the loud, continuous murmur over the pulmonary artery in the second intercostal space.

The operation consists in ligation or section of the duct. Although formerly only the ligation method was used, nowadays the method of section is advocated by various authorities, as reopening of the duct may occur when the ligature is not tight enough or slips off. A slight murmur after the operation does not necessarily mean a failure of the shunt. The operative mortality rate is low; the best age for operation is between 6 and 12 years.

Fifteen cases of patent ductus arteriosus are cited, in all of which ligation was without fatal result; one of the patients had to be operated on twice because of a relapse.

FROM THE AUTHOR'S SUMMARY.

Diseases of Nose, Throat, and Ear

AURICULOTEMPORAL SYNDROME: REPORT OF A CASE DEVELOPING IN EARLY CHILDHOOD WITH A REVIEW OF THE LITERATURE. W. PFEFFER JR. and S. S. GELLIS, Pediatrics **7**:670 (May) 1951.

The auriculotemporal syndrome is described. It consists of sweating and redness of the cheek brought on by eating in a person who has sustained injury to the auriculotemporal nerve in the region of the parotid gland. A case of the auriculotemporal syndrome is reported in a child who had been treated at 23 days for parotitis by incision and drainage.

The basic etiology of the syndrome is unknown. Certain physiological considerations are discussed. The condition is benign, nonprogressive, and one in which surgical division of the auriculotemporal nerve should be curative. Surgical interference in the parotid area should be avoided whenever possible to prevent the possible occurrence of the auriculotemporal syndrome.

FROM THE AUTHORS' SUMMARY.

CHANGES IN PHOSPHOLIPID AND CHOLESTEROL CONTENT OF BLOOD IN SCARLET FEVER. P. TOLENTINO and A. RAZZI, Pediatria **58**:528 (July) 1950.

Observations were made on 33 patients with scarlet fever. No definite changes in the blood cholesterol were observed. The phospholipid content of the blood usually was high during the first days of the disease and then fell to a subnormal level on about the fifth day; thereafter, it was within normal limits. The low values may be associated with hyperhemolysis during the acute exanthematous stage of the disease.

HIGGINS, Boston.

THE OCCURRENCE OF HYPOGLYCEMIA DURING ACUTE TONSILLITIS IN CHILDREN: REPORT OF TWO CASES. YUNG-EN KAO, SHU-FANG FENG, and YUNG-TSO YUAN, Chinese M. J. **69**:60 (Jan.-Feb.) 1951.

Two small children had hypoglycemic convulsions associated with acute tonsillitis. In both children caloric intake had been interfered with by anorexia, vomiting, and diarrhea. Increased metabolism and infection depleted their carbohydrate reserves. Both children recovered with proper treatment.

MACDONALD, Pittsburgh.

Diseases of Lungs, Pleura, and Mediastinum

COMPARISON OF PULMONARY HYALINE MEMBRANES IN VAGOTOMIZED RABBITS AND IN NEWBORN INFANTS. H. C. MILLER, F. C. BEHRLE, and D. M. GIBSON, Pediatrics **7**:611 (May) 1951.

Pulmonary hyaline membranes similar in appearance to those seen in newborn infants were found in 13 of 20 rabbits vagotomized bilaterally in the midcervical region. The time of appear-

ance of these membranes in relation to the operative procedure in the rabbits approximated closely the time of appearance of the membranes seen in the lungs of newborn infants in respect to the time of birth. In both species a polysaccharide aldehyde was regularly identified in the hyaline membranes. The similarity of the pulmonary lesion seen in vagotomized rabbits to that seen in newborn infants suggests that there may be factors common to both which are responsible for these pulmonary changes.

FROM THE AUTHORS' SUMMARY.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

RELATION OF O_2 CONSUMPTION TO CIRCULATION IN DIFFERENT STAGES OF INFANTILE MALNUTRITION. E. KERPEL-FRONIUS, F. VARGA, J. VONOCZKY, and K. KUN, Pediatrics **7**:623 (May) 1951.

The relation of oxygen consumption to circulation was studied in varying stages of infantile malnutrition. In severe "dystrophy" oxygen consumption and circulation are somewhat increased. In severe "atrophy" both cardiac output and oxygen consumption fall to lower values, the lowered metabolic need of the tissues, however, being met by a slower circulation. The condition is similar to that found in hypothyreotic patients. In athrepsia circulation collapses far below the metabolic need of the wasted organism; anoxia of the stagnating type ensues. Anoxia is, however, milder than in severe anhydremic circulatory shock, because the metabolic need of the tissues has decreased during the long atrophic and inanition period that preceded the terminal, athreptic stage of malnutrition. The poor circulation of the severely marantic infant may be an important factor in the high mortality rate found when such patients suffer intercurrent infections, especially in pneumonia and diarrheal disease.

FROM THE AUTHORS' SUMMARY.

OMPHALOCELE. C. M. BURGESS, J. PALMA, and W. A. MYERS, Pediatrics **7**:627 (May) 1951.

The authors report a case of congenital umbilical hernia, or "omphalocele," with recovery of an infant born with intrauterine rupture of the sac, strangulation of the bowel, and advanced general peritonitis. It was felt that the use of the polyethylene venous cannula in replacement therapy and the liberal use of antibiotics were the determining influences towards a successful outcome. The recent advances in the treatment of "omphalocele" are briefly reviewed.

FROM THE AUTHORS' SUMMARY.

CHYLOUS ASCITES IN INFANCY WITH REPORT OF A CASE WITH VITAMIN A ABSORPTION STUDIES. D. GRIBETZ and A. KANOF, Pediatrics **7**:632 (May) 1951.

There are only 25 cases of chylous ascites without concomitant effusion into the other body cavities. The etiology may be obstruction from without or stenosis of the duct, but it is unknown in the great majority of cases. Studies of the vitamin A absorption in this case indicate that there was a defect in absorption of chyle through the lymphatic pathways. Such absorption did take place when vitamin A was administered as an aqueous dispersion. In the rare cases caused by an obstruction, operative treatment may be indicated, but the greatest number of patients respond to paracentesis and supportive treatment.

FROM THE AUTHORS' SUMMARY.

AUREOMYCIN IN THE TREATMENT OF RUPTURED APPENDICES IN CHILDREN. B. S. JOSLIN and M. E. DRAKE, Pediatrics **7**:684 (May) 1951.

A report is given on the use of aureomycin as the sole antibiotic therapeutic agent in 16 cases of peritonitis or abscess complicating appendicitis occurring in children. In four of the cases surgery was postponed because of the child's condition. There were no deaths in this series.

Aureomycin appears to be the drug of choice when combined with surgery in treating appendicitis with abscess or peritonitis or to be used alone when surgery must be postponed. A satisfactory dosage schedule for aureomycin is given.

FROM THE AUTHORS' SUMMARY.

ANOREXIA AND LATENT KETONEMIA. F. COPELLO and A. GHIO, Lattante **22**:99 (Feb.) 1951.

A study of 13 children who presented the syndrome of anorexia and ketonemia suggests that the basis of the condition is of a constitutional, endocrinologic nature and not a perturbed hepatic insufficiency or dysfunction, as has been claimed by other clinicians.

HIGGINS, Boston.

HEPATIC CIRRHOSIS IN CHILDHOOD. GUSTAVO ROSS BRAVO, Rev. chilena pediat. **22**:52 (Feb.) 1951.

Four cases of Laennec's, or portal, cirrhosis, three of biliary cirrhosis, and two observations of Marchand's cirrhosis are reported. The last two cases are the first of that type to be analyzed in the national pediatric literature.

FROM THE AUTHOR'S SUMMARY.

INTESTINAL INVAGINATION IN CHILDHOOD. RENE ARTIGAS NAMBRARD, Rev. chilena pediat. **22**:60 (Feb.) 1951.

The diagnosis of intussusception must be based on the clinical findings of colicky abdominal pain, pallor, vomiting, rectal blood, and a palpable mass. A barium enema must be administered systematically as an element in the diagnosis, and it must be remembered that a negative result does not eliminate the possibility of an intussusception.

The treatment of choice must be surgical, as it is the most complete and objective one. A barium enema under pressure might be used as a therapeutic measure in very early cases, and if there is the slightest doubt as to the results obtained, it must be followed with surgery. Every patient given a barium enema must remain under strict medical surveillance.

As a suturing material the author recommends a nonreabsorbable one. During the postoperative period, plasma, blood, amino acids, antibiotics, and small fractionated feedings should be given. The author's statistics have improved appreciably with the use of these new therapeutic procedures.

FROM THE AUTHOR'S SUMMARY.

MECONIUM ILEUS: CYSTIC FIBROSIS OF THE PANCREAS. OSCAR CORREA B., ALFREDO VARGAS, and HELMUT JAEGER, Rev. chilena pediat. **22**:74 (Feb.) 1951.

A case of meconium ileus, which is the first to be described in Chile, is reported. A 2-day-old infant was admitted with the history of projectile vomiting, abdominal distention, and lack of passage of meconium. Because of an increase in symptoms, operation was decided upon on the third hospital day.

A marked dilatation of the small intestine, especially of the ileum, was found, with loops filled with inspissated, putty-like meconium, and there was hypoplasia of the large bowel, which looked like a probe, with a maximum diameter of 5 mm. The infant died 30 hours after operation, and at autopsy pathologic changes were noted in the pancreas, characterized by pronounced perilobular fibrosis, abnormalities in the lobular and acinar structures, and cysts. The case is briefly discussed.

FROM THE AUTHORS' SUMMARY.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS: REPORT OF TWO CASES OCCURRING IN SIBLINGS. T. T. HUANG, Chinese M. J. **69**:64 (Jan.-Feb.) 1951.

There is evidence for a genetic factor in the etiology of pyloric stenosis. Huang supports this evidence by reporting the disease in two siblings, one a boy, one a girl.

MACDONALD, Pittsburgh.

CONGENITAL MEGACOLON. J. STOVNER, Nord. med. **42**:1262 (July 29) 1949.

Stovner reports three cases of congenital megacolon in children, ages 8 years, 16 months, and 4 years, who were operated on by retroperitoneal subdiaphragmatic splanchnicectomy and sympathectomy on both sides. The results were excellent. In all three cases the bowel action became normal. Early operation is recommended, before secondary fibrotic changes destroy the neuromuscular mechanism.

WALLGREN, Stockholm, Sweden.

CELIAC DISEASE. ANDERS THO, Nord. med. **42**:1762 (Nov. 11) 1949.

The author reviews the cases of 54 patients with celiac disease who were treated at the pediatric clinic of the University of Oslo from 1940 to 1948. Admissions increased markedly from 1946 on. In most cases the disease manifested itself in the second half of the first year of life. Hypochromic anemia was present in 43% of the cases, and manifest or latent avitaminosis, particularly deficiency of vitamin D and K, was common. Folic acid was administered to eight patients without effect. The mortality rate during the hospitalization period was 4%. Therapy is discussed in detail.

WALLGREN, Stockholm, Sweden.

THYROID TREATMENT IN CELIAC DISEASE. OLOF ELGENMARK, Nord. med. **44**:1313 (Aug. 25) 1950.

In order to prevent a retardation in the development of the ossification centers in children with celiac disease, the author has treated five patients with thyroid hormone, with good results; the course of the disease was shortened. As the iodine of the thyroxin is obtained from the food stuffs resorbed in the intestine, it was assumed that iodine, like other salts, was not absorbed in sufficient amount to satisfy the requirement. The excretion of iodine in the urine did not comply with this theory. There was also the possibility that iodine could not be bound in the iodine-storing organs. The author intends to study this problem by means of iodine isotopes.

WALLGREN, Stockholm, Sweden.

ON THE OPERATIVE TREATMENT OF PYLORIC STENOSIS. C. C. WINKEL SMITH, Ugesk. læger **110**:483 (April 22) 1948.

Of 531 patients with pyloric stenosis treated conservatively at five children's hospitals in Copenhagen, 17 died (3.2%). The average stay in the hospital was 74 days. Of 23 patients operated on, none died, and the average stay at the hospital was two weeks.

WALLGREN, Stockholm, Sweden.

Nervous Diseases

OBSERVATIONS ON AN INFANT WITH TYPICAL GUILLAIN-BARRÉ SYNDROME. E. GHETTI and L. MARTONI, Clin. pediat. **32**:649 (Dec.) 1950.

An infant of 8 months presented the typical Guillain-Barré syndrome, having the symptoms of meningoencephalitis with a high protein content but only five cells in the spinal fluid, a hypercholesteremia, an enlarged liver, and a slightly positive indirect van den Bergh reaction. It is unusual to find this syndrome in so young a child. The belief is expressed that the etiology of the syndrome is a virus infection, but not necessarily one due to a specific virus.

HIGGINS, Boston.

SUBDURAL HEMATOMA AND FRACTURES OF THE LONG BONES. J. MENEGHELLO and J. HASBUN, Rev. chilena pediat. **22**:80 (Feb.) 1951.

The authors present a case of an infant with several fractures of the long bones associated with a subdural hematoma. The cause was not established. They stress the frequency of purpuric manifestations in patients with subdural hematoma with fractures.

FROM THE AUTHORS' SUMMARY.

MERCURY INUNCTION DURING AND AFTER CEREBRAL DISEASES ESPECIALLY DURING CHILDHOOD. LUDWIG SAUER, Med. Klin. **46**:478 (April 13) 1951.

The author refers to the coming publication of the results of treatment with mercury inunction in 10 cases of chronic inflammatory forms of nonsyphilitic hydrocephalus in the *Archiv für Kinderheilkunde*. At present 30 patients have been treated. Short descriptions of six cases

concerning children 3 months to 13 years of age are given. In these restitution to norm was accomplished. On the whole, patients with light inflammatory remnants respond better than patients with more advanced lesions. Acrodynia did not develop in any case.

AMBERG, Rochester, Minn.

GUILLAIN-BARRÉ-NEEL SYNDROME AS A COMPLICATION OF ACUTE HEPATITIS. P. J. DRAGSTED, Nord. med. **43**:599 (April 7) 1950.

A few days after recovery from acute hepatitis a 12-year-old boy fell ill with typical radiculoneuritis of Guillain and Barré's type. Rapid recovery resulted. Ten years previously the boy had suffered from a similar syndrome, and the recovery was as rapid as the second attack. The author stresses that the syndrome was first described by a Danish neurologist, A. Neel, and therefore suggests that the disease be called Guillain-Barré-Neel syndrome.

WALLGREN, Stockholm, Sweden.

ON THE STREPTOMYCIN CONTENT OF THE SPINAL FLUID IN INTRAMUSCULAR STREPTOMYCIN TREATMENT. H. C. A. LASSEN and K. A. JENSEN, Ugesk. læger **110**:1069 (Sept. 16) 1948.

Lassen and Jensen studied 9 persons free from meningitis, 5 patients with Hemophilus influenzae meningitis, and 15 adults and children with tuberculous meningitis. In the meningitis-free group streptomycin could be demonstrated only once, in a 10-month-old baby, in which at some examinations traces of streptomycin were found. In contradistinction to this result, high levels of streptomycin were found in the intraspinal fluid of the patients with Hemophilus influenzae and tuberculous meningitis. Of 15 patients with tuberculous meningitis treated with intramuscular injections of streptomycin, eight died. The authors recommend the intramuscular treatment of tuberculous meningitis.

WALLGREN, Stockholm, Sweden.

HOFFMANN-WERDNIG SYNDROME. D. P. R. KEIZER, Maandschr. kindergeneesk. **18**:59, 1950.

Keizer reports the case of a girl 21 months old suffering from spinal muscular dystrophy (Hoffmann-Werdnig syndrome), known from birth. The symptoms developed after six months; there was no hereditary influence. The child had hyperkeratosis, blue scleras, and a dominant hereditary funnel chest. Treatment consisted in administration of testosterone and vitamin B complex; the provisional results were promising.

FROM THE AUTHOR'S SUMMARY.

Psychology and Psychiatry

VISUAL RETENTION TEST PERFORMANCE IN CHILDREN. ARTHUR L. BENTON and NANCY T. COLLINS, Arch. Neurol. & Psychiat. **62**:610 (Nov.) 1949.

Performance studies show that the visual retention test is not too difficult for children 8 to 16 years to perform. Performance showed a close relation to mental age, and it is felt that discrepancies between the results of the visual retention and verbal intelligence tests may have clinical significance.

About half the children with brain injuries who are of adequate general intelligence show defective performance of this test. It may thus be useful in detection of such injury and analysis of the extent of such injury.

MCGUIGAN, Evanston, Ill.

VALUE OF CONVULSIVE THERAPY IN JUVENILE SCHIZOPHRENIA. SOL LEVY and R. H. SOUTHCOMBE, A. M. A. Arch. Neurol. & Psychiat. **65**:54 (Jan.) 1951.

Juvenile schizophrenia tends to run a malignant course which is not influenced by convulsion therapy.

MCGUIGAN, Evanston, Ill.

DIAGNOSIS AND TREATMENT OF A CASE OF HYSTERICAL APHONIA IN A THIRTEEN YEAR OLD GIRL. J. L. BANGS and A. FREIDINGER, J. Speech & Hearing Disorders **14**:312 (Dec.) 1949.

A girl, age 13 years, IQ 87, had functional aphonia for seven years. The pattern of life of the parents in general was in the direction of neurotic deviation. Hypnosis was unsuccessful. Laryngeal musculature was flaccid. Ten and one-half weeks of therapy were sufficient to give propositional speech in all situations, and the child has remained with normal vocalization for two years.

PALMER, Wichita, Kan.

THE NEUROLOGICAL EVALUATION OF DELAYED SPEECH. WILLIAM G. PEACHER, J. Speech & Hearing Disorders **14**:344 (Dec.) 1949.

In a speech clinic dealing with children with delayed speech, adequate neurological and neuropsychiatric examinations are of tremendous importance.

PALMER, Wichita, Kan.

THE USE OF CLINICAL PSYCHOLOGICAL SCREENING TECHNIQUES BY AUDIOLOGISTS AND SPEECH PATHOLOGISTS. HELMER R. MYKLEBUST, J. Speech & Hearing Disorders **15**:129 (June) 1950.

The author suggests that a speech clinic should utilize certain psychological testing programs. These cover mental competence, social maturity, personality, motor ability, educational achievement, hearing, and vision. The author suggests preferential tests.

PALMER, Wichita, Kan.

THE MENTALLY SUBNORMAL AND SOCIAL MEDICINE. REGINALD BAILEY, Edinburgh M. J. **56**:396 (Sept.) 1949.

Recent surveys indicate that the numbers of mentally subnormal children in England, Scotland, and Wales are increasing. Bailey reports that the great majority of these children are found in families of the unskilled laboring class and in families above the average in size.

From an analysis of these surveys it seems probable that the average level of intelligence among the general population may be declining at a rate which might produce serious consequences if sustained. The problem thus posed to social medicine is real and urgent. Part of the solution is obviously economic in nature; part is in increased medical and social help for the mentally subnormal and inefficient mother. It is to be hoped that as the National Health Service develops these problems may be solved.

MACDONALD, Pittsburgh.

CLINICAL-PSYCHOLOGICAL STUDY OF A LITTLE "DOMESTIC TYRANT." M. SCHACHTER, Pédiatrie **37**:130 (Jan.-Feb.) 1948.

A 4½-year-old boy who had shown tyrannical, destructive, and maniacal tendencies for one year was studied by means of clinical examination and Rorschach tests. This method of approach led to an early recognition of the underlying causes of a psychological (inconsistent attitude of the parents), economic, and social nature as well as of the innate trends and characteristics of the patient.

GLASSER, Chicago.

LATE NEURO-PSYCHOLOGICAL DISORDERS COMPLICATING PNEUMOPATHIES OF THE INFANT. M. SCHACHTER, Schweiz. med. Wchnschr. **81**:334 (April 7) 1951.

The author reports eight patients 5 to 14 years of age who had had one or more attacks of pneumonia during infancy. In six of these the disease was accompanied with convulsions; in one case no history of convulsions was obtained, and one boy seen at the age of 5½ years never had had convulsions. This boy had no psychological disorders, but there was a cerebellar syndrome. All the other children presented mainly psychological disorders, with more or less mental retardation.

AMBERG, Rochester, Minn.

MYOPATHY OF MONGOLISM. L. PERALE, Clin. pediat. **32**:663 (Dec.) 1950.

Histological studies were made on the tissues obtained from muscle biopsies (gluteus maximus or quadriceps femoris) on 14 children (20 days to 5 years of age) with Mongolism. In 10 cases a waxy degeneration of some muscle fibers was observed; in a smaller number of cases there was a tendency for fragmentation of the muscle fibers; the elastic fibers in other cases appeared abnormal. These changes were clearly congenital, and they may have some relation to the clinical findings in Mongolism.

HIGGINS, Boston.

INVESTIGATION AND CRITICAL STUDY OF PSYCHIATRIC ABNORMALITIES IN ILLEGITIMATE CHILDREN AND UNMARRIED MOTHERS. S. QUADRI and G. POLLINI, Lattante **22**:90 (Feb.) 1951.

In a group of 349 unmarried mothers, sheltered in a foundling hospital at Imola, Italy, 61 (17%) either had evident psychiatric abnormalities or immoral traits, such as prostitution or lesbianism. In a group of 700 illegitimate children, 53 (8.7%) were not normal mentally or socially; 38 (71%) were children of mothers with psychiatric or immoral tendencies, while 15 were children of mothers of normal mentality.

These statistics emphasize that many unmarried mothers are not qualified for the maternal training and moral assistance of their children and should not legally be required to care for them.

HIGGINS, Boston.

MONGOLISM AND HEREDITY. GEORG V. BREDMOSE, Nord. med. **42**:1923 (Dec. 16) 1949.

A report of the families and relatives in 51 cases of Mongolism showed a greater disposition in Mongolism families to oligophrenia. The disposition to deaf mutism, still births, and abortions is also greater than among other types of mental deficiency. Three tables are included.

WALLGREN, Stockholm, Sweden.

PSYCHOSOMATIC PEDIATRICS. SVEND HEINILD, Ugesk. læger **110**:1147 (Oct. 7) 1948.

An investigation of the admitted patients at a children's hospital in Copenhagen showed that 52% of children above 2 years of age did not suffer from real organic disease but rather from psychosomatic illnesses. The author discusses at some length the future development of pediatric psychiatric and psychologic work. He recommends the use of personnel trained in child psychology in pediatric wards and that more stress be put on the psychologic education of nurses. He warns against the separation of pediatric psychiatry as an independent specialty of pediatrics.

WALLGREN, Stockholm, Sweden.

Diseases of Genitourinary Tract

THE MORPHOLOGICAL BACKGROUNDS OF "GENUINE LIPOID NEPHROSIS." ELI MOSCHCOWITZ, Am. J. M. Sc. **216**:146 (Aug.) 1948.

The fundamental clinical phenomena of "lipoid nephrosis" are here reviewed and their genesis outlined. The primary factor is a prolonged hypoproteinemia. The hypoproteinemia is the result of a persistent proteinuria consequent to an increased permeability of the glomerular capillary walls, which is not always explainable histologically with our current technical methods. The hypoproteinemia, and especially hypoalbuminemia, is responsible for the edema and anasarca and for the low protein content of the exudate. In addition, the hypoproteinemia is probably indirectly responsible for the low basal metabolic rate, by creating an edema which acts as a suit of clothes preventing the dissipation of heat. This explanation is based on the demonstration that integumentary thickenings of whatever nature are usually accompanied with a low basal metabolic rate. The lipemia represents in all probability a compensatory phenomenon.

Evidence has been submitted to show that anatomical "lipoid nephrosis" represents nearly always one of the biological progressions of a glomerulonephritis, in which the conventional productive changes have either disappeared or not developed. In other instances it may be the result of extrarenal factors in which a hypoproteinemia ensues. Clinical "lipoid nephrosis" and

anatomical "lipoid nephrosis" are by no means synonymous. In the last analysis, "nephrosis" is not a disease in the sense that it has a consistent background in either morbid anatomy or etiology. Instead of employing a generic term to cover a multitude of unrelated morphological backgrounds, accuracy of thought would be promoted by ascribing the best available descriptive term for each renal disorder.

HENSKE, Omaha.

CONGENITAL POLYCYSTIC DISEASE OF THE KIDNEY: REVIEW OF THE LITERATURE, AND DATA ON 207 CASES. J. E. RALL and HOWARD M. ODEL, Am. J. M. Sc. **218**:399 (Oct.) 1949.

Clinical data are presented on 207 proved cases of congenital polycystic disease of the kidney, and certain common features are emphasized. A more optimistic attitude toward such patients is suggested by an average age at death of almost 50 years. Necropsy data in 46 cases of polycystic disease of the kidney reveal a frequency of unilateral polycystic disease, the common occurrence of associated congenital malformations, and differential features between infantile and adult polycystic disease of the kidney.

HENSKE, Omaha.

CARTILAGE IN THE KIDNEY. JOHN A. BIGLER and W. PRICE KILLINGSWORTH, Arch. Path. **47**:487 (May) 1949.

Report of findings at autopsy in kidneys of patients ranging in age from 4 days to 12 years is made. Either one or both kidneys in each case showed congenital developmental defects microscopically. Islands of cartilage were seen in one kidney in each case. The kidney in each instance was hypoplastic and also sometimes cystic. The authors explain the presence of cartilage as the result of metaplasia of the mesodermal embryonal tissue which forms the kidney. This would explain, too, why so much connective tissue, as well as smooth and striated muscle, is found in hypoplastic kidneys. According to Gruber, such a hypothesis could also be used to explain the occurrence of mixed tumors of the kidney. The authors state that cartilage has never been found in normal kidneys.

HAW CHAN, San Francisco.

PERITONEAL LAVAGE IN THE TREATMENT OF ANURIA IN CHILDREN. HENRY SWAN and HARRY H. GORDON, Pediatrics **4**:579 (Nov.) 1949.

Three children with acute anuria treated by peritoneal lavage and two others from whom such treatment was withheld are reported. Peritoneal lavage should be reserved for the treatment of a progressing uremic state associated with an acute, yet probably reversible, anuria of renal origin. The procedure, when suitably indicated, is effective for removal of nitrogenous waste products and may prove lifesaving.

Technical aspects of the method are discussed, and the use of variation of the dextrose concentration in the lavage fluid as a means of controlling water retention is demonstrated.

Peritoneal lavage is a complex, expensive, yet effective method of partially simulating the kidney glomerulus. The absence of tubular function in anuric patients who are receiving peritoneal lavage makes management of their acid-base balance a difficult problem.

FROM THE AUTHORS' SUMMARY.

UNILATERAL MULTICYSTIC KIDNEY IN INFANTS. MARK M. RAVITCH and MARSHALL C. SANFORD, Pediatrics **4**:769 (Dec.) 1949.

Four infants are reported with unilateral replacement of the kidney by large cysts. These cases and four similar ones found in the literature show (*a*) a large abdominal mass producing pressure symptoms only; (*b*) a normal contralateral kidney; (*c*) progressive increase in size of the mass; (*d*) adequate renal function after resection of the involved kidney.

In the four cases of the authors' and in the first four cases cited from the literature the process of organogenesis in one kidney seemed to have gone completely awry. In none of them was there any semblance of renal architecture, cortical substance, papillae, calyces, or pelvis, although a ureter-like cord was noted in several cases. This is very different from the condition

obtaining in congenital polycystic kidney, which is almost always bilateral and in which the fundamentally normal renal architecture is merely distorted by the numerous cysts.

FROM THE AUTHORS' SUMMARY.

RENAL CARBONIC ANHYDRASE IN PREMATURE AND MATURE INFANTS. R. DAY and JANE FRANKLIN, Pediatrics **7**:182 (Feb.) 1951.

The carbonic anhydrase activity in the kidneys of premature infants was studied because it was thought that if the renal enzyme is as deficient as that of the blood, inefficiency in acidification of urine might result. In contrast with the blood, postmortem specimens of kidneys of premature infants were found to exhibit carbonic anhydrase activity similar to that found in kidneys from older infants and adults.

FROM THE AUTHORS' SUMMARY.

TISSUE CHANGES IN THE NEPHROTIC SYNDROME. C. L. FOX JR., and L. B. SLOBODY, Pediatrics **7**:186 (Feb.) 1951.

Analyses of skeletal muscles, obtained at autopsy from six children with the nephrotic syndrome, reveal losses of from one-fourth to two-thirds of the potassium content each unit of dry weight or cell solids. The phosphorus content is only moderately reduced. These muscles have gained large amounts of water, sodium, and chloride in ratios approximating extracellular fluid.

The muscle values are compared with other types of potassium loss from muscle, e. g., after experimental potassium deprivation, desoxycorticosterone therapy, alkalosis, and muscle trauma.

Since potassium is the intracellular cation, its depletion may be associated with important effects on intracellular anions, enzymes, or catalysts, and, together with cellular hydration and hypotonicity, it contributes to the physiologic alterations found in this syndrome.

Analyses of kidneys from these patients reveal somewhat similar changes; liver in contrast showed minimal alteration.

FROM THE AUTHORS' SUMMARY.

NEPHROTIC SYNDROME IN RATS. W. HEYMANN and H. Z. LUND, Pediatrics **7**:691 (May) 1951.

Chronic renal disease was produced in 235 rats 4 to 5 weeks old, of the Long-Evans strain, by the intravenous injection of nephrotoxic serums obtained from rabbits.

Massive proteinuria, largely without hematuria, was noted immediately. Severe edema and ascites were observed in 35% of the animals within the first two to three weeks. Thirty-two per cent died within the first two weeks. A spontaneous cure of the disease occurred in 30%, and chronic renal disease that lasted in some instances as long as 13 months was observed in the remaining animals. Of 125 sick rats, 74% remained normotensive. A fluctuating and moderately severe hypertension was noted in the remaining 26%.

The blood chemistry revealed marked hypoproteinemia and hyperlipemia in the earliest phase. This subsided slowly as the disease progressed but did not reach normal values as long as the disease persisted. With a few exceptions the creatinine concentration remained normal during all phases of the disease. Marked azotemia was frequently obtained in severe disease at onset. It subsided regularly within the first two months, and slight degrees of azotemia in late stages of the disease were noted in approximately 50% of the rats.

A histologic analysis was obtained in 119 sick, 12 recovered, and 31 control rats. By correlating the chronologic order of clinical evidence with the pathologic picture, the following conclusions were drawn: 1. The nephrotoxin produces primarily a degenerative lesion with changes in glomeruli and tubules. 2. The degenerative phase may subside, or it may be followed at variable intervals with a variable degree of fibrous proliferation in the glomerular tufts and capsules. Whether this fibrosis of glomeruli is a direct repair of damaged glomeruli or a result of abnormal glomerular function could not be determined. 3. In the degenerative phase the lesion produces the "nephrotic" syndrome. In the proliferative phase, depending on the degree, there are hypertension and uremia.

In symptoms and course, in the deviation of the blood chemistry, and in the morphology of the renal lesion this disease in rats simulates the nephrotic syndrome as observed in infants and

children. One and the same experimental procedure produces the disease in rats in its so-called pure and mixed forms.

FROM THE AUTHORS' SUMMARY.

NOCTURNAL HAEMOGLOBINURIA (MARCHIAFOVA-MICHELI SYNDROME). M. SALAT and M. D. GHANEM, J. Roy. Egyptian M. A. **32**:548 (June-July) 1949.

Two cases of Marchiafova-Micheli syndrome are presented. Attacks were aggravated or precipitated in one case by psychic fatigue or emotional upheaval. In one case nocturnal microfilaria were found, and the question is raised of a possible etiologic relation. Both cases showed hemolysis with in vitro acidification with hydrochloric acid and carbon dioxide, supporting Ham's theory of an autohemolysin produced by a shift in the pH toward the acid side.

McGUIGAN, Evanston, Ill.

ARE THERE INDICATIONS FOR SURGERY IN ACUTE GLOMERULAR NEPHRITIS IN CHILDREN? P. BERTOYE, G. ROMAGNY, J. MARTIN, and LANTERNIER, Pédiatrie **37**:224 (March-April) 1948.

A survey of statistical material shows that in general a good prognosis can be given in cases of acute hemorrhagic nephritis in children, yet a certain number will pass into chronicity. Surgical intervention to improve the circulation of the kidney was suggested to prevent the development of sclerotic changes. Present statistics indicate that only a few cases of acute hemorrhagic nephritis develop into chronic cases, whereas the majority progress to complete cure. Furthermore, there are no known indications at present to foretell which case will develop into chronic nephritis and which will not. Only such an early indication may give surgical treatment a chance of intervening before permanent damage has occurred. The authors contend that at the present status of our knowledge the treatment of hemorrhagic nephritis should remain strictly medical.

GLASER, Chicago.

FAMILIAL NEPHRITIS. H. HERZOG, Schweiz. med. Wchnschr. **81**:349 (April 14) 1951.

On the basis of reports in the literature and the author's own observations, the problem of familial nephritis is discussed. There has been an increased incidence of familial nephritis of different causes, particularly in association with angina, scarlet fever, and impetigo contagiosa. Two siblings in each of three families were subjects of nephritis. The ages varied from 2½ to 7 years. Familial nephritis is considered a clinical entity, and it is assumed that the kidneys of these patients are particularly sensitive to toxins.

AMBERG, Rochester, Minn.

NEW THERAPEUTIC APPLICATIONS OF GLUTAMIC ACID. G. LODI, Lattante **22**:103 (Feb.) 1951.

In connection with the treatment of mentally retarded children with glutamic acid, it was observed that of 41 children with enuresis at the onset of medication, 31 no longer wet the bed four to six months later.

HIGGINS, Boston.

COMBINED THERAPY OF PENICILLIN AND A SYNTHETIC ANTIHISTAMINE DRUG IN GLOMERULONEPHRITIS OF CHILDREN. V. BAFFI, Pediatria **58**:198 (March) 1950.

Five children 20 months to 10 years of age, with glomerulonephritis, were treated with penicillin intramuscularly and an antihistamine drug orally. It is claimed that quicker and better therapeutic results followed administration of the two drugs together than the administration of either of them separately.

HIGGINS, Boston.

RETENTION OF URINE IN CHILDHOOD CAUSED BY A VESICAL DIVERTICULUM. JAN KUČERA, Pediat. listy **5**:41, 1950.

The author reports a case of mechanical retention of urine caused by a diverticulum of the bladder in a boy of 8 years. The congenital diverticulum had compressed the lower urinary tract, causing a lasting residuum and increasing the intravesical pressure. This resulted in

further overdistention of the diverticulum, hypertrophy of the bladder wall, with following dilation of the bladder, the ureters, and the right renal pelvis (the left kidney being atrophic), and with atrophy of the renal parenchyma. The urosepsis resulted in the death of the child because the parents refused an early operative treatment.

The author mentions briefly various causes of mechanical urine retention in children and enumerates the diseases which cause a mechanical retention of the urine in childhood. He explains the origin of the described case of diverticulum as an anomaly of the development of the terminal part of the left Wolffian duct.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL MEGALOURETER WITH HYDRONEPHROSIS. E. VANĚČEK and A. BUČEK, Pediat. listy **5**:45, 1950.

A case of congenital bilateral megaloureter and hydronephrosis with megalobladder and hyperplasia of the prostate in a 5-week-old boy is reported. There was no evidence of organic obstruction. These anomalies are considered to be developmental defects, an excess formation due to faulty anlage, which resulted in congenital hyperplasia.

FROM THE AUTHORS' SUMMARY.

TWISTED OVARIAN CYST IN A NEWBORN INFANT. P. Y. SUN, Chinese M. J. **69**:52 (Jan.-Feb.) 1951.

P. Y. Sun reports a simple ovarian cyst with a twisted pedicle, found in the right iliac fossa of a stillborn infant. The cyst was 4.5 cm. in diameter.

MACDONALD, Pittsburgh.

URETHRAL VALVES IN AN INFANT. JÖRGEN B. DALGAARD, Nord. med. **42**:1963 (Dec. 23) 1949.

A newborn boy who showed obstruction of the urinary tract died at the age of 14 days. At autopsy hydronephrosis, dilatation of the ureters, and hypertrophy of the bladder wall were found. In the prostatic urethra below the seminal colliculus two pocket-shaped valves were found which obviously were the cause of the obstruction. Catheterization was easily performed in the beginning but later became difficult, and vesical puncture had to be performed.

WALLGREN, Stockholm, Sweden.

THE RENAL CLEARANCE WITH THIOSULPHATE AND INULIN IN CHILDHOOD. BJARNE ANDERSEN and FOLKE TUDVAD, Nord. med. **43**:286 (Feb. 17) 1950.

Thirteen children with normal kidneys and three children with diseased kidneys were examined. In the normal children inulin clearance was 75 to 105 (mean 90.5) ml. a minute per 1.73 m.² of surface. Thiosulphate clearance was 124 to 242 (mean 162.7) ml. a minute per 1.73 m.² of sulfate. In patients with nephritis inulin clearance was 58.8 to 102.3 (mean 81.8) ml. a minute per 1.73 m.² of surface, and thiosulphate clearance was 90.5 to 252 (mean 155.8) ml. a minute per 1.73 m.² of surface.

WALLGREN, Stockholm, Sweden.

INTERSEXUALITY. K. E. SJØLIN and H. RAHBEK SØRENSEN, Nord. med. **44**:1173 (July 21) 1950.

The authors report a case of a girl 3½ years old with bilateral inguinal hernia in whom testes with epididymides were palpable. Herniotomy was performed on the left side. Biopsy of testis showed infantile testicular tissue. The left testis was transplanted to an area between peritoneum and the abdominal musculature.

WALLGREN, Stockholm, Sweden.

SIX CASES OF WILMS' TUMOR IN CHILDREN. AKSEL K. F. JACOBSEN, Nord. med. **44**:1244 (Aug. 4) 1950.

Jacobsen reports six cases of embryonal carcinosarcoma of the kidney (Wilms's tumor) in children aged 2 months to 7½ years. Three of them were girls. Five of the children died three

and one-half to 15 months after the beginning of the symptoms. The oldest child was operated on after one month of preoperative x-ray treatment and was found healthy six and one-half years after operation. The main symptom was abdominal tumor. Only one patient displayed symptoms of renal disease (hematuria).

WALLGREN, Stockholm, Sweden.

NANISMUS RENALIS. FOLKE TUDVAD, Ugesk. læger **110**:987 (Aug. 26) 1948.

Tudvad reports three cases of renal dwarfism in children aged 2, 5, and 2 years in which the renal disease had been diagnosed at 2 weeks, 10 months, and 2 years of age. There were polyuria, isosthenuria, and continuous (two cases) or intermittent (third case) albuminuria. Nonprotein nitrogen was normal for a long time and eventually became increased, and in the third case it ended in uremia. Phosphorus content was increased or normal, and calcium content was normal or slightly increased. Rachitic changes were present but slight. The renal lesion in the first case was supposed to be a congenital malformation; in the second case it was probably due to chronic glomerulonephritis, and in the third case (the patient was the only one that was dead at the time of publication), at postmortem examination chronic pyelonephritis was shown.

WALLGREN, Stockholm, Sweden.

Diseases of Ductless Glands; Endocrinology

EXOPHTHALMIC GOITER IN CHILDREN: TREATMENT WITH PROPYLTHIOURACIL. ARNOLD S. JACKSON and HAROLD B. HALEY, Am. J. M. Sc. **218**:493 (November) 1949.

Twenty-six cases of exophthalmic goiter have been observed in children ranging in age from 8 to 16 years. Symptoms and treatment have been discussed, especially the results of thiouracil and propylthiouracil treatment in eight patients so treated. The following conclusions seem warranted:

Depression of white blood cells must be carefully watched for in the use of thiouracil and propylthiouracil. In four of eight patients treated with these drugs white cell counts below 5,000 developed, although there were no serious complications. Propylthiouracil is much safer than thiouracil, which should no longer be used.

These drugs have a goitrogenic action, as evidenced by two cases in which, although toxicity was relieved, the continuing large size of the gland made it necessary to perform thyroidectomy.

Early diagnosis in some cases may be difficult, for two reasons: (1) atypical symptomatology and (2) the masking of the clinical picture by previous treatment.

Individual response to these antithyroid drugs is uncertain in children, and there is no rule to determine in which cases they will be successful. At present, the best place for these drugs is probably in preoperative preparation or in patients for whom it may be necessary to delay operation. The fact that in only one patient with hyperthyroidism was the disease apparently permanently arrested by propylthiouracil indicates that operation is still the method of choice in the treatment of these patients. Iodine should be given to all patients prior to and after operation. Its use is especially indicated after propylthiouracil to decrease the vascularity of the gland and reduce bleeding at operation.

HENSKE, Omaha.

THE NECESSITY OF TESTIS AND THYROID HORMONES FOR THE MAINTENANCE OF THE SEROUS TUBULES OF THE SUB-MAXILLARY GLAND IN THE MALE RAT. B. GRAD and C. P. LEBLOND, Endocrinology **45**:250 (Sept.) 1949.

Since the time, about a century ago, when research on the salivary glands began in earnest, most of the investigations dealing with these organs indicated that they were under the control of the nervous system. Therefore, it came as a surprise to learn that the male sex hormone plays an important role in the maintenance of the serous tubules of the submaxillary glands of mice.

The object of the study here reported was to examine the endocrine control of the serous tubules, which, in addition to mucous acini, constitute the secretory portion of the submaxillary gland of the rat.

The results are as follow:

1. Control animals in which testes and thyroids are extirpated show an atrophy of the serous tubules. 2. Treatment of such animals with testosterone alone has little or no effect on the size and granule content of the cells of the serous tubules. 3. Treatment with thyroxin alone has little effect on the size and granule content of the cells of the serous tubules, but it restores the number of these cells to normal. 4. A combined treatment with both hormones restores a normal size and granule content as well as a normal number of the cells of the serous tubules.

In comparison with the major role of the testis and thyroid hormones in the maintenance of the serous tubules, nervous influences such as those occurring in the course of feeding and fasting have only a minor effect.

JACOBSEN, Buffalo.

THE EFFECT OF GROWTH HORMONE UPON LIVER AND KIDNEY D-AMINO ACID OXIDASE AND UPON MUSCLE SUCCINIC ACID DEHYDROGENASE. O. H. GAEBLER, J. C. MATHIES, and L. PALM, Endocrinology **45**:267 (Sept.) 1949.

Since enzymes are proteins, and may indeed constitute a major part of the protein in cells, several relations between them and the growth hormone are conceivable. The concentrations of the two enzymes discussed in this paper do not change during induced growth, so there is no indication of a relation to the growth hormone differing from that of other tissue proteins.

JACOBSEN, Buffalo.

THE EFFECTS OF PITRESSIN AND DESOXYCORTICOSTERONE IN LOW DOSAGE ON THE EXCRETION OF SODIUM, POTASSIUM, AND WATER BY THE NORMAL DOG. OTTO W. SARTORIUS and KATHLEEN ROBERTS, Endocrinology **45**:273 (Sept.) 1949.

It has been shown that there exists a physiological antagonism between the diuretic action of adrenal cortical hormone and the antidiuretic action of posterior pituitary hormone. An antagonism between the sodium and chloride-conserving effects of the former and the chloruretic and natriuretic effects of the latter has also been postulated. It has been suggested that the major disturbances in electrolyte and water metabolism of the adrenalectomized animal resemble an exaggerated effect of posterior pituitary antidiuretic hormone. As desoxycorticosterone is known to correct the disturbed electrolyte balance in Addison's disease without significantly altering the disturbed water balance, it seemed reasonable to predict the desoxycorticosterone would reduce the natriuresis but have no effect on the antidiuresis produced by the administration of vasopressin injection (pitressin®) to the normal animal. The data presented in this paper bear out these inferences.

JACOBSEN, Buffalo.

CYTOTOXIC ACTION OF HORMONES OF THE ADRENAL CORTEX ACCORDING TO THE METHOD OF UNSTAINED CELL COUNTS. ROBERT SCHREK, Endocrinology **45**:317 (Sept.) 1949.

The reactions of cells to x-rays and nitrogen mustard (methyl-*bis* or *tris* [2-chloroethyl] amine hydrochloride) have been studied previously by the method of unstained cell counts. This method has been used in this work to determine the effect of extracts and hormones of the adrenal cortex on cells of the thymus and of the bone marrow.

As a result of these experiments, the hypothesis is proposed that the extracts of the adrenal gland accelerate the normal degeneration and death of lymphocytes.

JACOBSEN, Buffalo.

ADRENOTROPHIC ACTIVITY OF HUMAN BLOOD. A. ALBERT, Endocrinology **45**:335 (Sept.) 1949.

The presence of corticotropin, or a substance or substances possessing adrenotrophic activity, has not been convincingly demonstrated in human urine. The authors have therefore turned their attention to the blood, in the hope that adrenotrophic material might be present in a concentration sufficiently high to be measured by current assay procedures.

Adrenotrophic activity has been demonstrated in the blood of patients with adrenal cortical insufficiency. Conclusive demonstration of adrenotrophic activity in the blood of normal subjects and of patients with adrenal cortical hyperfunction was not achieved. JACOBSEN, Buffalo.

IN VITRO EFFECT OF ADRENAL CORTICAL EXTRACT UPON LYMPHOCYTOLYSIS. OSCAR HECHTER and SELMA JOHNSON, Endocrinology **45**:351 (Oct.) 1949.

Little is known concerning the mechanism whereby adrenocortical hormones produce lymphocyte dissolution in vivo. There is evidence, however, that adrenocortical steroids do not act directly upon lymphocytes to produce lysis. The possibility is raised that the in vivo lymphocytolytic activity of adrenocortical hormones requires a factor present in lymphoid tissue. It has been found that adrenocortical extract is an effective lymphocytolytic agent in the presence of homogenates of lymphoid tissue but that adrenocortical extract is ineffective in serum, blood, or buffered saline solutions. Preliminary studies suggest that the lymphoid tissue cofactor is enzymatic. The lymphocytolytic reaction obtained with adrenocortical extract seems to be specific in the sense that none of the 10 crystalline steroids tested duplicate the results obtained with adrenocortical extract. JACOBSEN, Buffalo.

INACTIVATION OF POSTERIOR PITUITARY ANTIDIURETIC HORMONE BY THE LIVER. W. J. EVERSOLE, JAMES H. BIRNIE, and ROBERT GAUNT, Endocrinology **45**:378 (Oct.) 1949.

It has long been recognized that the liver bears some important relation to water metabolism. In experimental liver damage and in liver disease of man, water retention has been reported. The presence of antidiuretic substances in urine has been associated with liver dysfunction. The suggestion has been made that this may be the well-known neurohypophyseal antidiuretic hormone appearing in the urine, because it is not effectively inactivated by the damaged liver.

Experiments here reported indicate that the liver is one site of inactivation of the posterior pituitary antidiuretic hormone. JACOBSEN, Buffalo.

THE EFFECT OF TOTAL BODY X-RADIATION ON 17-KETOSTEROID EXCRETION IN DOGS. GEORGE HUGH LAWRENCE, Endocrinology **45**:383 (Oct.) 1949.

Attention has been drawn to alterations in adrenal cortical function in response to x-ray therapy. The urinary excretion pattern 17-ketosteroids was assayed in 11 dogs after exposure to minimal lethal dose of total body x-ray treatment. All animals exhibited a significant increase in steroid excretion at some time between the 5th to the 12th day following radiation treatment. JACOBSEN, Buffalo.

THE EFFECTS OF THYROXIN AND THIOURACIL ON THE TIME OF APPEARANCE OF OSSIFICATION CENTERS OF RAT FETUSES. ROBERT M. WEISS and CHARLES R. NOBACK, Endocrinology **45**:389 (Oct.) 1949.

The time of appearance of the ossification centers studied was not significantly altered in the 16-day-old rat fetuses the mothers of which were injected daily with 1 mg. of crystalline thyroxin from either the 6th or the 10th day after pregnancy.

The time of appearance of the same ossification centers was definitely delayed in the 16-day-old rat fetuses the mothers of which were fed on a diet containing 0.2 to 0.4% thiouracil from the date of pregnancy. JACOBSEN, Buffalo.

EXCRETION OF GLUCOCORTICOIDS IN THE NEWBORN. ELEANOR H. VENNING, J. PERLINGIERO RANDALL and PAUL GYORGY, Endocrinology **45**:430 (Oct.) 1949.

The adrenal gland of the newborn infant differs greatly from that of the adult person. At birth the adrenals are relatively large structures, and the cortex is composed of an outer or true cortical part and an inner part, the fetal cortex. This fetal cortex grows rapidly during

the last trimester of fetal life and at birth or just previous to birth begins to degenerate. Although numerous investigations have been carried out since the first observation of this phenomenon, in 1908, the function of the fetal cortex and the significance of its rapid involution are still not understood.

An attempt has been made to determine whether the fetal cortex produces glucocorticoids, those adrenal hormones which promote the conversion of body protein to carbohydrate. As glucocorticoids are excreted in urine, their measurement affords a relative means of evaluating the activity of the adrenal cortex with regard to this function.

Gradual increase in the excretion of glucocorticoids coincides with the rapid involution of the fetal cortex. This fact does not seem to support the suggestion that the fetal cortex of the newborn is elaborating glucocorticoids.

JACOBSEN, Buffalo.

SEVERE HYPOPROTHROMBINEMIA FOLLOWING PROPYLTHIOURACIL TREATMENT OF THYROTOXICOSIS. CHARLES G. CRADDOCK JR., DONALD SHOTTON, CHARLES L. CROCKETT, and BYRD S. LEAVELL, New England J. Med. **244**:549 (April 12) 1951.

Severe, temporary hypoprothrombinemia developed in a 16-year-old girl with thyrotoxicosis who was being treated with 100 mg. of propylthiouracil three times a day. The differential diagnosis of the source of the bleeding included the following: (1) hepatic damage due to the use of thiourea derivatives; (2) congenital idiopathic hypothrombinemia; (3) liver damage concomitant with, and because of, the thyrotoxicosis; (4) impaired absorption of vitamin K; (5) intravascular inhibition of prothrombin activity; (6) failure of prothrombin production by liver, and (7) drug intoxication with hypoprothrombinemia.

The last possibility above was decided upon, and the reasons for this and exclusion of the others are given. The mechanism of the bleeding was believed due to deficiency of V factor (AC globulin [Seegers]), an accelerator substance. Treatment included fresh human serum and whole blood, and subtotal thyroidectomy was carried out successfuly.

WHEELOCK, Denver.

VARIOUS PEDIATRIC ENDOCRINE PROBLEMS. W. A. REILLY, New Orleans M. & S. J. **103**:227 (Dec.) 1950.

Obesity and Mongolism are listed as nonendocrine problems, to differentiate them from the common endocrine diseases seen in practice. The latter include hypopituitarism, comprising adiposogenital dystrophy (Froehlich's syndrome), Levi-Lorain syndrome (characterized by dwarfism and congenital infantilism but no obesity), and Cushing's syndrome; hypothyroidism; hyperthyroidism; adrenocortical lesions, and ovarian agenesis. All are described very briefly and treatment mentioned.

MCGUIGAN, Evanston, Ill.

RAPID TRANSFORMATION OF CRETINS WITH LARGE DOSES OF THYROID. EDWARD E. BROWN, Northwest Med. **50**:22 (Jan.) 1951.

"The physician has within his grasp a potent agent for treating the cretin, namely, desiccated thyroid substance. Yet, only too often in his conservatism he administers insufficient amounts of this specific medicine. The pathetic spectacle of cretinism recorded here is the result of prolonged microdosage. With large doses of thyroid the cretin can be transformed in a short time to an alert, vivacious child."

With this introduction, the author presents two case histories illustrating his point. He further defines inadequate doses as those of 0.25 grain (0.015 gm.) to 1 grain (0.06 gm.) daily and more adequate doses as being up to 3 grains or more (0.19 gm.) of desiccated thyroid daily.

In conclusion he admits that toxic symptoms may be produced by an optimal dose of thyroid but states that the physician must take the responsibility of prescribing this large dose. To give less is to deprive the cretin of his only chance for full mental and physical development.

DOCTOR, Seattle.

BRAIN DAMAGE IN A JUVENILE DIABETIC PATIENT ASSOCIATED WITH INSULIN HYPOGLYCEMIA. L. I. GARDNER and GERTRUD C. REYERSBACH, Pediatrics **7**:210 (Feb.) 1951.

A case is described illustrating the relative ease with which cerebral damage may develop from insulin hypoglycemia in juvenile diabetic patients. Diabetes in this child began at 22 months of age, and repeated hypoglycemic episodes occurred on treatment with protamine zinc insulin alone. At 7 years of age the patient's mental age was 7 to 10 years, but he had an abnormal electroencephalogram and had become a behavior problem. Hypoglycemic insulin reactions continued, and within 10 months the patient showed gross mental damage with deterioration of language comprehension to the 2½-year level. The patient then began to have seizures unassociated with hypoglycemia and died at 12 years of age after a convulsion. It is pointed out that juvenile diabetic patients seem to be better on insulin therapy providing a higher ratio of crystalline to protamine zinc insulin than is commonly used for adults.

FROM THE AUTHORS' SUMMARY.

ALBERS-SCHONBERG DISEASE. S. B. DIMSON, Proc. Roy. Soc. Med. **42**:77 (Feb.) 1949.

A girl of 6½ months was admitted to the hospital with hydrocephalus, snuffles, enlarged liver and spleen, and apparent blindness. Roentgen examination of the skull showed posterior clinoids clubbed and sella turcica narrowed and no distinction between cortex and diploë. Ribs, clavicle, and bodies of vertebrae and pelvis were uniformly dense. Limbs showed clubbing of the ends of the long bones and ring-like shadows of increased density at the ends of the metacarpals and phalanges of the hands, less marked in the feet. Roentgenograms, investigations, treatment, progress, and a short discussion of osteopetrosis (Albers-Schönberg disease) accompany the report.

WILLIAMSON, New Orleans.

THE THYROID CLEARANCE RATE OF PLASMA AS A MEASURE OF THYROID ACTIVITY. N. B. MYANT and E. E. POCHIN, Proc. Roy. Soc. Med. **42**:959 (Dec.) 1949.

Methods are outlined for determining percentage of dose of iodine present in thyroid, urine, and plasma at any interval after administration. Normal and thyrotoxic subjects were compared as to iodine content of thyroid, renal clearance rate, and plasma concentration. In normal subjects an average of 25 ml. a minute of plasma is cleared of iodine, whereas in thyrotoxicosis ratios always exceed 100 ml. a minute and usually 150 ml. a minute. Clearance in myxedema is a few milliliters a minute only and in nontoxic goiter is normal or only slightly elevated. Renal clearance for iodine averages 30 ml. a minute and is unchanged in thyrotoxicosis. There is normally a wide variation in the renal clearance for iodine in normal subjects. Two graphs are included.

HEARD, Monterey, Calif.

URINARY EXCRETION OF RADIO-ACTIVE IODINE AS A MEASURE OF THYROID ACTIVITY. A. STUART MASON, Proc. Roy. Soc. Med. **42**:961 (Dec.) 1949.

Iodine determinations made on total urine collected from 6 to 24 hours after ingestion of radioactive iodine revealed definite variations between normal subjects (10 to 25%), thyrotoxic patients (2 to 4.5%), and myxedema (26 to 33%) patients. The patient with the mildest thyrotoxicosis showed a value of more than three times that of the mean normal. Observations on patients with mild hyperthyroidism resulted in obtaining values between those for high normal subjects and thyrotoxicosis patients. Either previous treatment with iodine or diminished renal function causes manifest errors in determination of thyroid function by this method. Deficiencies in dietary iodine intake explain variations in normal subjects. Bulk samples of urine collected from 6 to 24 hours after a dose of radioactive iodine reveal a clear-cut difference between normal and thyrotoxic persons.

HEARD, Monterey, Calif.

CLINICAL USE OF RADIO-ACTIVE IODINE. RUSSELL FRASER, Proc. Roy. Soc. Med. **42**:962 (Dec.) 1949.

Fully developed pictures of thyroid overactivity and thyroid underactivity are easily recognized by use of radioactive iodine. Measurements of urinary excretion rate of radioactive

iodine show definite ranges for normal, thyrotoxic, and hypothyroid persons. Urinary excretion of radioactive iodine was measured in clinically proved thyrotoxicosis cases, and in almost all instances the results agreed with the clinical diagnosis. Radioactive iodine has much to recommend it in possible diagnostic uses but has little if anything to commend it in treatment. Four graphs are included.

HEARD, Monterey, Calif.

DIABETES IN CHILDHOOD. ERIC B. SIMS, Clin. Rep. Adelaide Child. Hosp. **1**:177 (May) 1949.

An unusually comprehensive discussion of diabetes in children is presented, with excellent descriptions of the physiology and metabolism involved. Discussions of diet, treatment, and general management of the diabetic child are clear, concise, and up-to-date.

MCGUIGAN, Evanston, Ill.

HYPERTHYROIDISM IN THE FIRST YEAR OF LIFE. P. M. S. FISCHER, South African M. J. **25**:217 (March 31) 1951.

A review of the literature is presented, only five cases of hyperthyroidism in infants in the first year of life having been reported. The author presents a further case in an infant, born of a thyrotoxic mother, in whom the symptoms began at the age of 3 days. The infant was cyanotic, irritable, had a temperature of 104 F., and a pulse rate of 240. He was markedly dehydrated. By the age of 8 days the infant showed some exophthalmos and a visible and palpable goiter. Exophthalmos and goiter persisted for three and one-half months.

Treatment was largely supportive, the addition of strong iodine (Lugol's solution) having no noticeable effect. The author feels that the disease is self-limited.

MCGUIGAN, Evanston, Ill.

FAMILIAL RECURRING HYPERTROPHY OF THE THYMUS. J. MARIE, P. SERINGER, and G. SEE, Presse méd. **56**:680 (Sept. 29) 1949.

A baby of 3 months had presented severe attacks of crying and extreme agitation two or three times a week for six weeks. The thymus was found to be enormously hypertrophied, requiring nine roentgen treatments over a period of a month. The first dose was 50 r, the others were 100 r. The attacks ceased for four months but then reappeared. Roentgenograms then showed a return of the large thymus shadow. Another series of roentgen treatments caused the disappearance of the shadow, and attacks ceased altogether.

Three years later a newborn sibling showed a marked enlargement of the thymus, with no clinical symptoms. Roentgen treatment caused the disappearance of the thymus shadow.

DAFFINEE, Melrose, Mass.

LAURENCE-MOON-BIEDL SYNDROME. JULIO A. BAUZA and FERNANDO GASTELU, Arch. pediat. Uruguay **22**:171 (March) 1951.

The authors describe a case of Laurence-Moon-Biedl syndrome studied at the endocrinologic outpatient department in the Pereira-Rossell Hospital of Montevideo.

No family history was elicited. The following signs were observed: adiposity, hypogonadism, mental retardation, pigmentary retinitis, and unilateral polydactylism. Mental retardation was very evident. Thyroid treatment caused a slight improvement.

FROM THE AUTHORS' SUMMARY.

SENILITY IN CHILDHOOD, ESPECIALLY GILFORD'S PROGERIA. H. R. WIEDEMANN, Ztschr. Kinderh. **65**:670, 1948.

The author collected and analyzed the reports of the world literature on senility in childhood and illustrated the article extensively. The differentiation of true progeria from other conditions producing a senile appearance of the child is discussed in detail. Although other etiologic

causes are discussed, the most widely accepted cause for this most unusual disease is a genetic disturbance of the mesenchyme. The possibility of certain analogies with other mesenchyma' disturbances, such as arachnodactyly (Marfan's syndrome), cleidocranial dysostosis, and osteogenesis imperfecta, are considered.

GLASER, Chicago.

CONTINUOUS UNEVENLY DISTRIBUTED CYANOSIS CAUSED BY AN ECCENTRIC HYPERTROPHY OF THE THYMUS IN A NEWBORN INFANT. I. HEČKO, K. HOREČNÝ, and J. PENIAŽKA, Pediat. listy **5**:8, 1950.

The authors explain the uneven distribution of cyanosis, manifested locally, especially on the head and neck, in a newborn infant that died on the 16th day after birth from sepsis by the pressure of the eccentrically hypertrophied thymus (enlarged to the right side) on the vena cava superior. The results of the clinical, pathologic, anatomical, histological, and x-ray examination proved the diagnosis.

FROM THE AUTHORS' SUMMARY.

THYROTOXICOSIS IN A 5-YEAR-OLD GIRL. H. VEFLINGSTAD, Nord. med. **41**:648 (April 8) 1949.

Veflingstad reports a case of thyrotoxicosis in a 5-year-old girl with symptoms dating one year back with typical signs. She had a keen appetite, exophthalmia, goiter, tachycardia, and great motor activity. She was 115 cm. tall and had a body weight of 19 kg. A subtotal strumectomy was successfully performed.

WALLGREN, Stockholm, Sweden.

SEROFIBRINOUS PLEURISY DUE TO LYMPHOSARCOMA OF THE THYMUS IN AN INFANT. N. TUNESTAM, Nord. med. **43**:382 (March 3) 1950.

Tunestam reports a case of lymphosarcoma of the thymus in a boy aged 9 months. The illness started with a large pleuritic exudate on the left side. Thoracentesis gave 150 ml. of yellow, thin, opalescent exudate, containing 2,000 cells per cu. mm., of which 84% were mononuclears and 16% polymorphonuclears, and no red blood cells. The boy died shortly afterward and postmortem examination showed tumor of the thymus gland that had invaded pericardium and pleura on the left side.

WALLGREN, Stockholm, Sweden.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

SOLITARY (UNICAMERAL) BONE CYST. ARTHUR G. JAMES, BRADLEY L. COLEY, NORMAN L. HIGINBOTHAM, Arch. Surg. **57**:137 (July) 1948.

Solitary bone cyst generally attracts attention during the first and second decades of life. It usually occurs in the proximal part of the metaphysis of a long bone, the humerus being the bone most commonly involved. A history of trauma at the onset of symptoms is often obtained from the patient. The symptoms are ordinarily mild until a pathologic fracture occurs. Objective findings on physical examination are meager and nonspecific. Slight tenderness may be present over the cystic area. Some limitation of motion may be present because of pain. The diagnosis is made from the roentgenograms. The cause of solitary bone cyst is not known. Twenty-six cases are reported. The treatment was surgical in all cases with the exception of one. Recurrences took place in four cases.

KAISER, Rochester, N. Y.

EARLY TREATMENT OF METATARSUS VARUS (ADDUCTUS). A. B. SIRBU and BEN COLLOFF, Pediatrics **4**:810 (Dec.) 1949.

Early diagnosis of metatarsus varus will result in uniformly good results by conservative orthopedic measures. It is characterized by fixed adduction of the forefoot, a rounded outer border of the foot, frequent association of splayfoot, and some degree of cavus. The hindfoot is normal in the preambulant child but may go into talipes valgus in the older child. Roentgen studies before and after correction are a necessary adjunct in the treatment. This deformity is not self-correctable and requires definitive therapy.

The most effective treatment is a multiple wedging cast technic. Correction is obtained in 10 to 12 weeks, and appliances to maintain the correction are usually not necessary after that. A series of 33 patients is recorded, 20 with bilateral deformities. Girls predominate slightly in this series, which is the reverse of the incidence in clubfoot. Correction of the deformity has been obtained in all but one case by conservative orthopedic measures.

FROM THE AUTHORS' SUMMARY.

VOLUMETRIC AND MICROSCOPIC PATTERN OF BONE MARROW IN NORMAL INFANTS AND CHILDREN: II. CYTOLOGIC PATTERN. P. STURGEON, Pediatrics **7**:642 (May) 1951.

With the use of the described bone marrow aspiration and concentration (volumetric) technique, the percentage distribution of the major categories of cells appears to follow the general pattern reported from studies of bone marrow in infants and children by the direct smear techniques.

The percentage distribution of nucleated cells from sternal and iliac aspirations in the age range studied showed no apparent differences between the two sites nor influence of age on the data.

In normal children as young as 1½ years of age and with advancing age thereafter, an increasing number of tibial aspirations show a very low percentage of normoblasts (0-5) and a majority of lymphocytes and segmented neutrophiles.

FROM THE AUTHOR'S SUMMARY.

News and Comment

ANNOUNCEMENTS

Coming Examinations to be Held by the American Board of Pediatrics, Inc.—The American Board of Pediatrics, Inc., will hold written examinations under local monitors on Friday, Jan. 11, 1952. This is the only written examination which will be given during 1952. The oral examinations for 1952 will be held on Feb. 1, 2, and 3, in New York; in April, in St. Louis; on May 3, 4, and 5, in Washington, D. C.; in late June, in San Francisco; in October, in Chicago, and in late November, in Boston.

The Leonard Parsons Memorial Lectureship.—The Leonard Parsons Memorial Lectureship has been instituted at Birmingham, England, in honor of the late Sir Leonard Gregory Parsons of that city.

Those wishing to contribute to this worthy fund may send their contributions to the Dean of the Faculty of Medicine, The Medical School, University of Birmingham, Birmingham 15, England.

The Jacobi Fund.—The Section on Pediatrics of the American Medical Association at the meeting held in June, 1951, decided to reactivate the Jacobi Fund, inactive since World War II.

The Jacobi Fund had its inception at a meeting of the Section in 1929 for the purpose of defraying the expenses of guest speakers, thereby promoting research and education in the field of pediatrics. It was named the Jacobi Fund to memorialize the name of the "father of American pediatrics," Abraham Jacobi, of New York. Jacobi, a former president of the American Medical Association, was the first chairman of the Section on Diseases of Children, in 1880.

With no solicitation of funds for many years, the principal of the Jacobi Fund now amounts to $5,532, invested in government bonds, and the revenue is insufficient to carry out the purpose for which it was created. It is intended with the use of the fund to stimulate interest in the Section meetings by the invitation of guest speakers as well as to reimburse our Director of the Scientific Exhibit and our Delegate to the House of Delegates of the American Medical Association. Both of these positions require a considerable amount of work, time, and travel expense, and it is unreasonable to continue the practice of having the members who are elected to these positions bear all the travel and hotel expense necessary to carry out the duties of their offices.

It becomes necessary, therefore, to replenish the monies we have spent, to reimburse distinguished guests, and to expand our program. We are inviting all pediatricians to make a contribution of five, ten, or more dollars to the fund. This is a deductible item on income tax returns. Please make checks payable to the Jacobi Fund and send to Hugh L. Dwyer, M.D., Custodian, 315 Nichols Rd., Kansas City 2, Mo.

DEATHS

Death of Prof. Ruggero Vaglio.—Prof. Ruggero Vaglio, of Naples, died on April 4, 1951. He was for 17 years assistant to Prof. Rocco Jemma, and since 1927 he had been director of the Brefotrofio di Napoli. He was one of the editors of the pediatric journals *Il Lattante* and *Minerva Pediatrica.*

Death of Dr. Louis Ribadeau-Dumas.—Dr. Louis Ribadeau-Dumas, the eminent French pediatrician, died recently. His loss will be keenly felt, in France and throughout the world generally, because of his contributions to pediatrics.

PERSONAL

Appointment for Dr. Charles F. McKhann.—Dr. Charles F. McKhann, of Cleveland, has been made Acting Medical Director for United Cerebral Palsy, New York.

Appointment for Dr. Lytt I. Gardner.—Dr. Lytt I. Gardner, Department of Pediatrics, Johns Hopkins Medical School, has been named Associated Professor of Pediatrics at the State University of New York Medical Center at Syracuse University, Syracuse, N. Y.

STANDARD NOMENCLATURE OF DISEASES AND OPERATIONS

Fourth Edition

The American Medical Association announces the publication of the Fourth Edition of "Standard Nomenclature of Diseases and Operations." Changes in the new edition have been as much as possible kept to a minimum. Nevertheless, advancing knowledge has made necessary a complete revision of the section on the psychobiologic unit, diseases of the hemic and lymphatic systems, and tumor etiology. A completely new feature of this edition is the inclusion of code numbers of the International Statistical Classification of Diseases, Injuries, and Causes of Death, parenthetically in the body of the book, and a cross reference of International and Standard code numbers as an appendix. The new edition is being published for the Association by The Blakiston Company (Philadelphia) and will be available Jan. 2, 1952.

CORRECTION

In the August issue, page 210, in the abstract of "Penicillin Therapy in Diseases of Children from an Experience with 122 Cases, N. Carrara and B. Krainer, *Il Lattante* **20**:65 (Feb.) 1949," the last sentence should read "In certain diseases other antibiotics are recommended in addition to the penicillin, such as streptomycin in pertussis and a sulfonamide in meningococcus meningitis."

Also on page 210 of the August issue, in the abstract of "Italian Contribution to Pediatrics in 1949, F. Lo Presti-Seminerio, *Il Lattante* **21**:756 (Dec.) 1950," the last sentence should read "The most extensively treated subjects in this list are the streptomycin treatments of tuberculosis and the blood dyscrasias, especially familial erythroblastic anemia (Cooley's anemia)."

Book Reviews

Werdnig-Hoffmann's Infantile Progressive Muscular Atrophy. By Sven Brandt. Price, 20 Danish kronen. Pp. 328, with 39 figures. Ejnar Munksgaard, 6, Nörregade, Copenhagen, Denmark, 1950.

The book is an exhaustive review of the subject of generalized muscular flabbiness in infancy and childhood, with special reference to the well-defined syndrome, Werdnig-Hoffmann infantile progressive muscular atrophy, to the more heterogeneous group that, in the author's opinion, falls into the category of amyotonia congenita (Oppenheim's disease), and to the rarer examples of what appears to be muscular dystrophy. The first chapter is a review of the literature, following which the writer presents a survey of 131 Danish cases in which these diagnoses, or equivalent ones, had been recently made in various clinics.

The writer investigated by personal interview with the families the 71 cases in which death had occurred and personally examined 60 patients. During this undertaking 25 secondary cases were found, making a total material of 156 cases.

Diagnostic criteria are discussed and the importance of properly performed biopsy stressed as the most important single laboratory aid. Electromyography is disappointing as a diagnostic tool. Family history of other similar lesions is in favor of progressive muscular atrophy. The presence of the condition at birth or even in utero (reduced fetal movements) does not exclude progressive muscular atrophy. Sustained motor improvement lasting over many months is, in the author's opinion, valid evidence against progressive muscular atrophy, but minor improvement over a period of weeks or a few months may appear in cases subsequently shown pathologically to be progressive muscular atrophy. Fibrillation is always taken by the author as evidence of active degeneration of lower motor neurons and therefore as diagnostic of progressive muscular atrophy in the presence of generalized weakness.

The investigations of the author show that of the total material, 112 cases fall into the group of progressive muscular atrophy. Among 73 cases originally diagnosed as amyotonia congenita, the disease proved to be progressive muscular atrophy in 38. All the 25 secondary cases are examples of the latter disease.

Progressive muscular atrophy may be rapidly progressive, ending in death in the first year or two, and in these instances muscular atrophy is difficult to demonstrate clinically because of the plumpness of the affected infants. Many of these show very symmetrical positions of the extremities, especially the arms, with tendency toward contractures.

Cases of more slowly progressive disease may permit survival up to 15 or 20 years, and in these atrophy of the proximal muscle groups may be striking. Death occurred prior to 1 year in 56%, prior to 4 years in 80%, and survival to between 12 and 20 years occurred in 8%. The earlier in life the weakness appears, the more malignant the course.

The histology of the nervous system and muscles is discussed. In 14 instances the autopsy findings are described by the author, and two other autopsy reports are added from hospital records. The only constant abnormalities found in progressive muscular atrophy are loss of anterior-horn cells of the spinal cord and medulla and demyelinization of the anterior roots. These changes take place without evidence of inflammation or vascular lesions. In a few instances other cell groups, such as those of Clarke's column, the dorsal-root ganglia, and cell groups in the cortex, are mildly involved in a similar process.

Thirty-eight muscles from 25 affected children are described. Biopsy material must be carefully selected to obtain muscle undergoing active degeneration and must be specially handled. In these circumstances, patch atrophy of muscle fibers with marked variation in cross-sectional diameter is indicative of progressive muscular atrophy. Diffuse irregular atrophy may occur in primary muscular disease or in progressive muscular atrophy, and in older children increase in fat and supporting tissue may obscure the picture.

Heredity is the most important etiologic factor, and on a statistical basis the author adduces moderately conclusive evidence that the disease is inherited as a recessive characteristic. In a few families, however, there is a suggestion of modified dominance. On the basis of animal experiments by others, Brandt attempts to relate the disease to an inherited inability to utilize vitamin E.

Treatment has so far been totally unavailing. Attempts to prevent the disease by treatment of mothers during pregnancy with vitamin E failed to prevent the disease in their offspring. Once the weakness is manifest, changes in the nervous system are already beyond the reversible stages, and as is to be expected, the use of various vitamins and drugs produces no changes.

Eugenic considerations are fully discussed, and a table giving the likelihood of transmission of the disease by relatives of affected persons is presented. This table presumes that the disease is inherited as a recessive characteristic and that it is a rare one in the population at large.

A large portion of the book is occupied by the case material and genealogical charts of each case of progressive muscular atrophy. A card index applicable to all known cases in Denmark is on file with the University Institute of Human Genetics in Copenhagen.

Differential diagnosis is discussed for a group of 29 children, in which the original diagnoses of amyotonia, progressive muscular atrophy, or progressive muscular dystrophy is revised to a completely different type of disease. Cerebral palsies, idiocy, multiple neuronitis, dermatomyositis, and spinal-cord tumors are common causes of mistakes. The absence of obstetrical cord injury is striking in relation to American experience.

Finally, a somewhat heterogeneous group of 13 cases with diffuse flabbiness, otherwise unexplained, remains; to it Brandt applies the diagnosis of amyotonia congenita. In some the weakness completely disappeared, and, at present, the persons are competitive; in others the weakness has remained stationary or improved so little that they are ineffective cripples. Brandt feels that this group is so variable that it cannot represent a nosological entity.

The book is a very thorough attempt to clarify a question about which controversy rages. It points out usefully how much commoner is progressive muscular atrophy than amyotonia congenita and calls for diagnostic and prognostic care in relation to the latter diagnosis. It may well be that many clinicians would favor the inclusion of the 8% of cases of very chronic progressive muscular atrophy with a life expectancy of 15 to 20 years in the latter category. The paucity of pathological examinations in such cases and their complete absence in amyotonia congenita of a sort diagnostically satisfying to the author makes a final appraisal on scientific terms impossible.

Year Book of Pediatrics, 1950. Edited by Henry G. Poncher, M.D., with the collaboration of Julius B. Richmond, M.D.; Isaac A. Abt, M.D., Editor Emeritus. Price $5.00. Pp. 504, with 104 illustrations. The Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1950.

The mid-century marks the fiftieth anniversary of the Year Book of Pediatrics. The occasion is observed by the inclusion of 17 authoritative guest editorials. They are concise, three to four pages in length, and they cover a wide range of subjects. For the second time the editor has included a general discussion of pediatric advances of the year. In it he makes documented reference to fourteen new developments. They include not only the significant advances in pediatric theory and practice but also the growing trend toward a broadening of the responsibilities of pediatricians in the fields of education and community health. The section affords a stimulating introduction to the book. As in the past, the abstracts are well selected. Editorial comment has been extended. In a number of instances it has been expanded into a concise review of recent trends. These new features give one a sense of the past and future of the subjects discussed, as well as their present status. The 1950 year book remains the outstanding pediatric guide for the general practitioner, an excellent refresher for the busy pediatrician, and a convenient springboard for the more intensive investigator.

A Study of Diphtheria in Two Areas of Great Britain. By Percival Hartley, W. J. Tulloch, M. Anderson, W. A. Davidson, J. Grant, W. M. Jamieson, C. Neubauer, R. Norton, and G. H. Robertson. Price, 4 shillings. Pp. 158, with 81 tables. His Majesty's Stationery Office, York House, Kingsway, London, W.C. 2, England, 1950.

This study is thought-provoking and casts some doubt on our criteria for the measurement of immunity. It is a thoroughly performed report, attempting to explain why diphtheria has not been completely eradicated in certain population groups of Great Britain that have been immunized.

The following factors were examined: 1. There is no correlation between circulating antitoxin and attack rate. 2. Mitis, intermedius, and gravis types produce toxin which basically is

identical. 3. The mortality rate in previously immunized groups is nil. 4. Some persons respond poorly to stimuli (toxoid). 5. Approximately 70% of persons in an epidemic area have to be immune before an epidemic can be brought under control.

This report should be valuable to those interested in the public health and pediatric aspects of the control of diphtheria.

Annual Review of Medicine, Vol. I, 1950. Edited by W. C. Cutting, M.D., H. W. Newman, M.D., and others. Price, $6.00. Pp. 484. Annual Reviews, Inc., Stanford, Calif., 1950.

This is the first volume on medicine of the Annual Review series. The editors state that their purpose is to review the various fields of medicine regularly and that since some of the various fields scarcely need a yearly review, the more active fields will be reviewed annually, while other sections will be reviewed only every two or three years.

The various authors have taken pains to avoid mere uncritical listings of papers and to make their scope broad and to include their own critical assessments of work discussed. As a result, the articles are highly readable and are informative and effective presentations of medical advances. Lengthy bibliographies are included at the close of the articles.

The list of authors is impressive, with outstanding authorities responsible for each chapter. The plan is to use different authors in each edition, to avoid presenting a single viewpoint.

This book is as its title states a review of medicine. Its purpose appears to be well fulfilled. The *Annual Review of Medicine* can be read with profit by all physicians. It is highly recommended.

Williams Obstetrics. Tenth edition. By Nicholson J. Eastman. Price, $12.50. Pp. 1176, with 659 figures. D. Appleton-Century-Crofts Company, Inc., 35 W. 32d St., New York 1, 1950.

The new (tenth) edition of "Williams Obstetrics," prepared by Nicholson J. Eastman, is a worthy successor to the previous editions of this classic text. The subject matter has been slightly rearranged, to advantage, and has been extensively revised to include many fundamental contributions which have been made since the last edition in 1945. Most of the sections dealing with the newborn child have been completely rewritten and include many important additions. Notable among these is the discussion of hemolytic disease of the newborn, which presents a detailed and most lucid discussion of modern concepts of Rh incompatibility. The sections dealing with prematurity, the normal newborn, and injuries sustained by the infant during labor have been similarly extended. Other sections which have been entirely rewritten, and which present full discussion of recent advances, are those dealing with toxemia of pregnancy, the endocrine glands, the estimation of pelvic capacity, the forces concerned in labor, the physiology of the placenta, the management of pregnancy complicating specific medical diseases, and many others. All of these changes combine to make the book entirely comprehensive, authoritative, and up-to-date. The magnificent drawings of the late Max Brödel, which have been gems of this text since the first edition, have been retained, and some 200 new and well-executed illustrations have been added. The author's vast clinical and teaching experience, his many contributions to the art and science of obstetrics, and his easy, lucid style of writing contribute much toward making this current edition of Williams Obstetrics outstanding among medical textbooks.

Tuberculosis and Other Problems of Pediatrics. By Arvid Wallgren, M.D. Price, $2.25. Pp. 108, with 7 charts. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1950.

Dr. Arvid Wallgren, Professor of Pediatrics at the Royal Caroline Medical Institute, Stockholm, Sweden, was the invited guest to give the tenth series of the Abraham Flexner Lectures at Vanderbilt University. During his two months' stay at Vanderbilt University Dr. Wallgren gave five lectures, and it is these that make up the volume described.

The titles of the lectures are as follows: "General Trends in Combating Tuberculosis in Childhood," "BCG Vaccination," "One Thousand Cases of Erythema Nodosum," "The Illegitimate Child in Sweden," "Studies on Infantile Hypertrophic Pyloric Stenosis." Dr. Wallgren is a well-known authority on tuberculosis in children, so it is with special interest that one reads what he has to say about the methods employed in Sweden for the control of tuberculosis

among children. He is a staunch advocate for the use of BCG vaccination, and pediatricians and public health workers in this country, where BCG has not been widely accepted, will be interested in his arguments. Erythema nodosum in Sweden is associated with a positive tuberculin reaction in 90% of the cases. Rheumatic fever was the cause of the eruption in only two of the 1,000 cases cited by Dr. Wallgren. The illegitimate child and its unwed mother get a far better break in Sweden than they do in this country. American pediatricians will be surprised to learn that in Sweden pyloric stenosis is treated conservatively with atropin methylnitrate and gastric lavage. Of 350 patients, only five were operated on, and no deaths occurred among the last 120 patients treated conservatively.

Most American pediatricians are familiar with Dr. Wallgren's high standing among the scientists and pediatricians of the world, and many have had the pleasure of hearing him on the lecture platform at some of our own pediatric meetings. A vote of thanks is due the Vanderbilt University for making it possible for the pediatricians of the country to share in these lectures.

The Management of the Patient with Severe Bronchial Asthma. By Maurice S. Segal, M.D. Price, $3.50. Pp. 158, with 16 illustrations and 7 tables. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

This monograph of the American Lecture Series on the management of the patient with severe bronchial asthma is an interesting and provocative one. The author makes it clear that asthma is a composite disease consisting of physiologic, pathologic, and psychic disturbances and demonstrates the ineffectiveness of attempting to treat the many facets from a single approach. His emphasis on the fact that the finding of a single remedy for so complex a syndrome is remote is most laudable.

The complicating factors of disturbed physiology and secondary pathologic sequelae make it obvious that little real benefit can accrue to the patient from treatment that does not focus upon them. Dr. Segal does an excellent job in making the reader cognizant of the multiplicity of conditions that have to be continually borne in mind when treating the severe asthmatic. The section covering psychotherapy is to be commended.

The entire gamut of therapeutic agents is skilfully covered, and one gets the full impact of the multiplicity of drugs and measures that have been advocated in the treatment of asthma. It becomes apparent that no rule of thumb can be applied, and because so many different therapies have been suggested, it is obvious that few are really good and none is best in all cases. This stems from the fact aforementioned that asthma, particularly in the adult, is a complex condition.

The therapeutic measures suggested are based on extensive laboratory studies and the author's personal observations of over 500 patients with asthma. Protecting drugs, methods of sedation, supportive therapy, antispasmodic therapy, the use of gases, the management of infection, and preventive measures are covered.

This book is of value for the pediatrician, for it should impress upon him the life-long suffering the person must endure if asthma is untreated in childhood. The pediatrician has the opportunity to treat the young asthmatic seriously, and it is up to him to make every effort to reduce the number of adult asthmatics. It is quite obvious from reading this volume that the treatment of severe asthma in the adult is truly a difficult job, and not always satisfactory.

The book is well gotten up, and it should be a useful addition to the pediatrician's library.

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2. Karelitz, S., Does Modified Measles Result in Lasting Immunity? Jour. Pediat., 36:697, June 1950.

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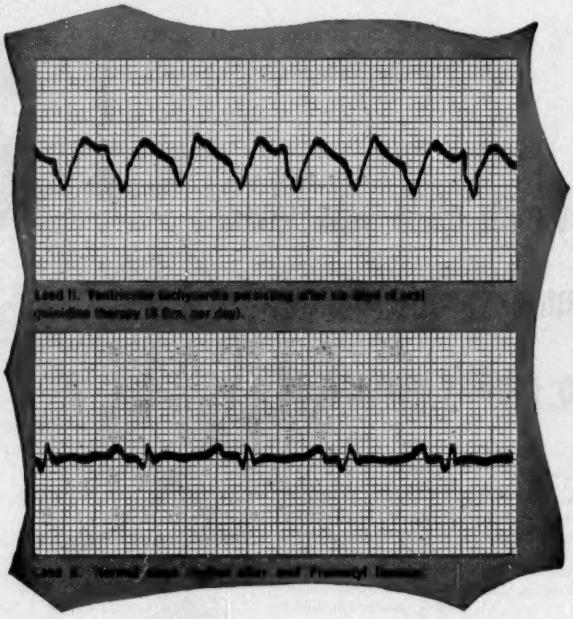

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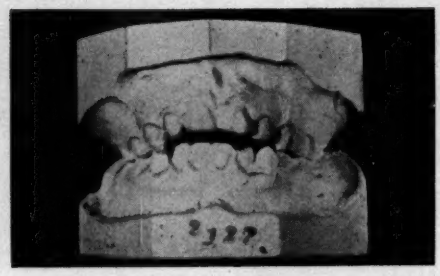

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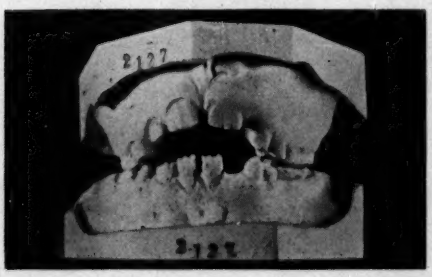

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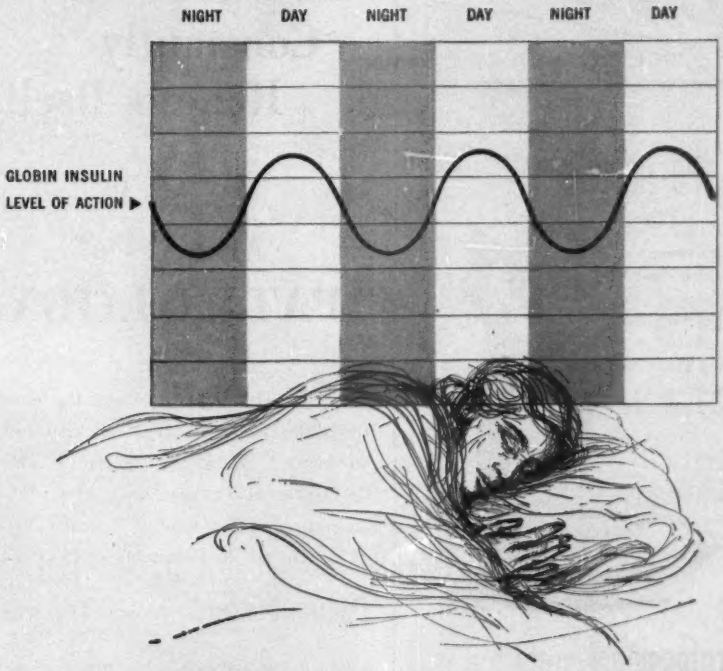

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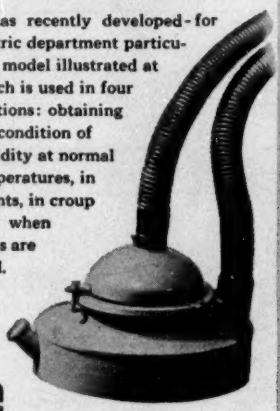

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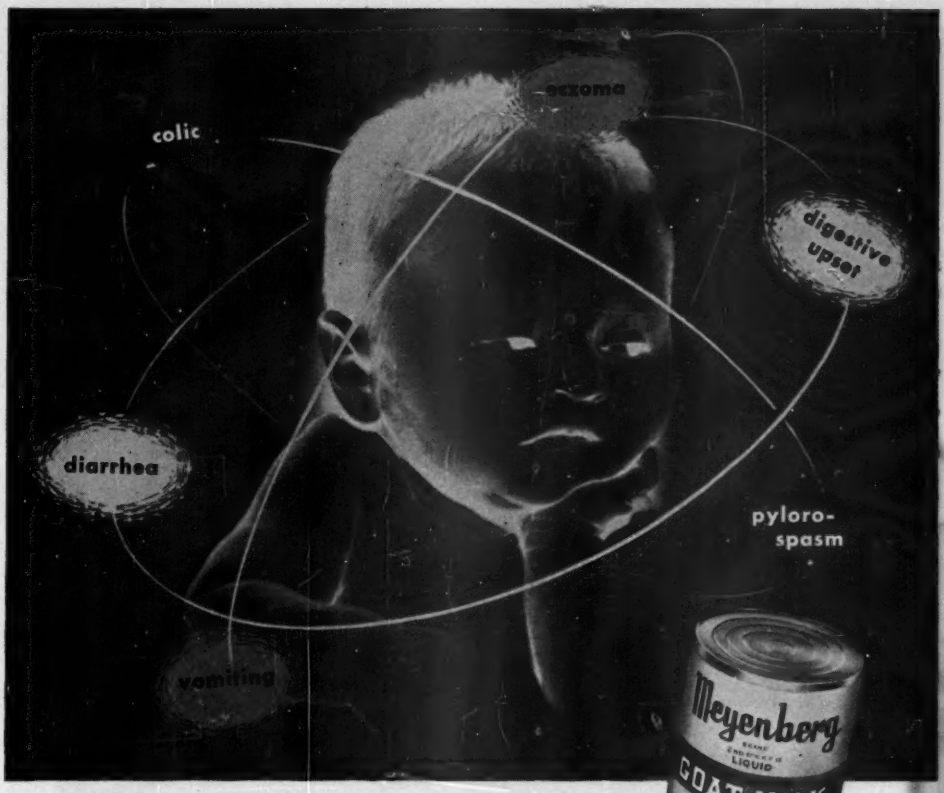

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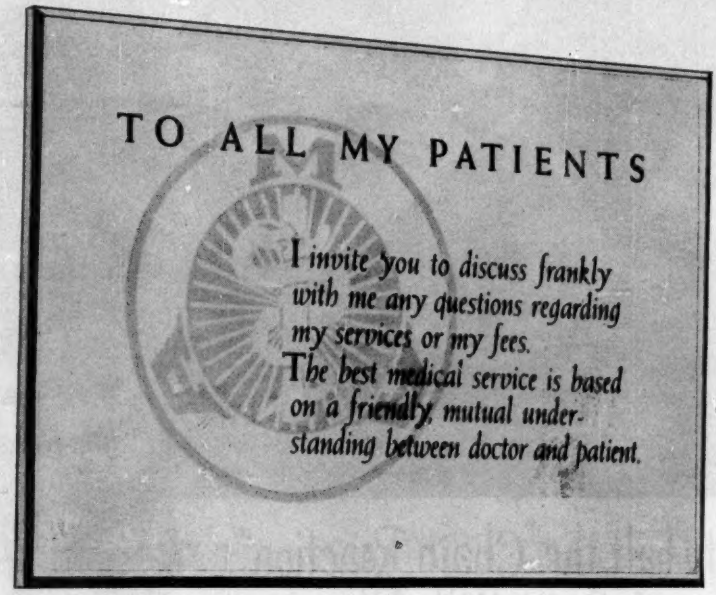
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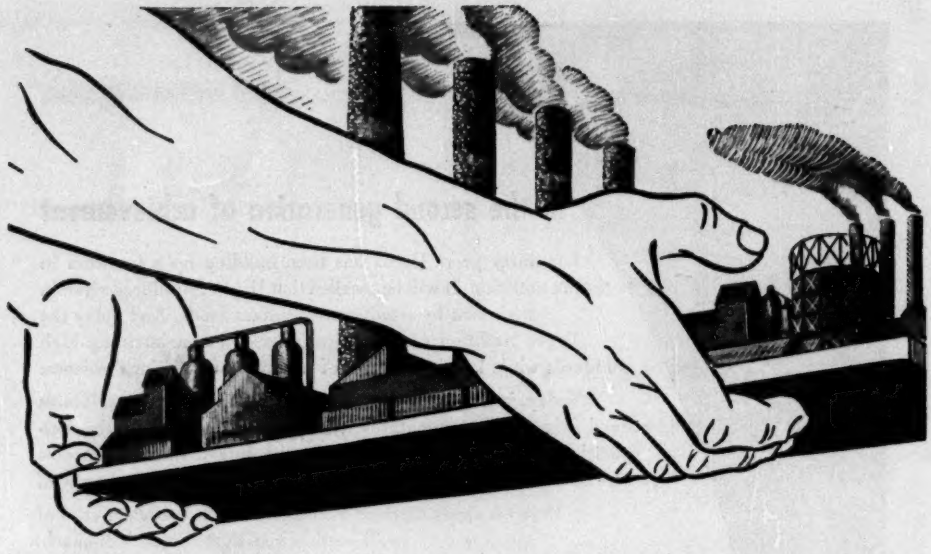

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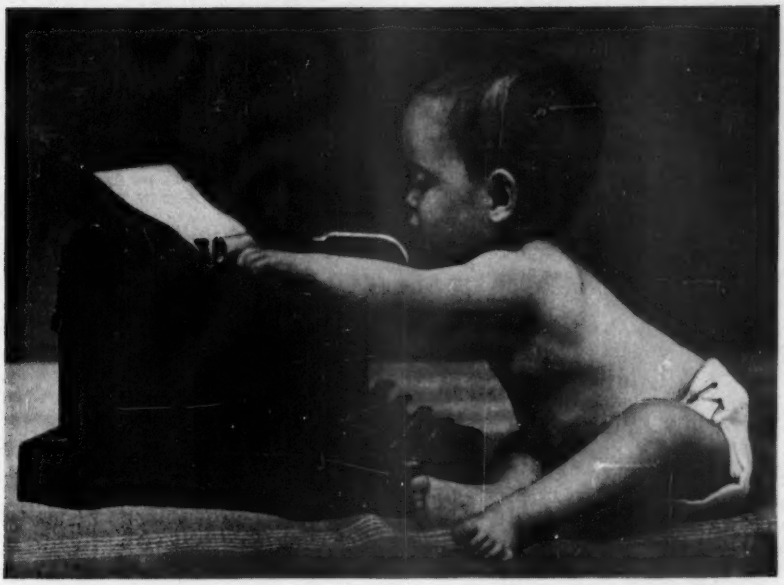

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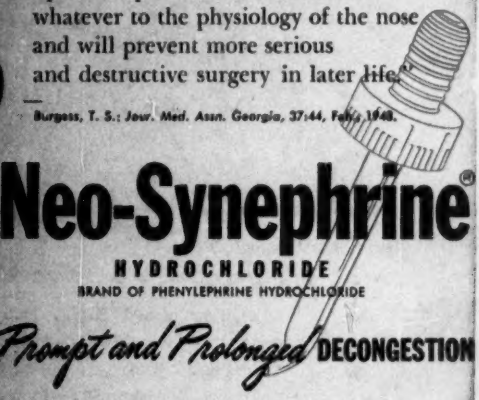

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